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# Rhodium(II) catalyzed synthesis of macrocycles incorporating oxindole *via* O–H/N–H insertion reactions

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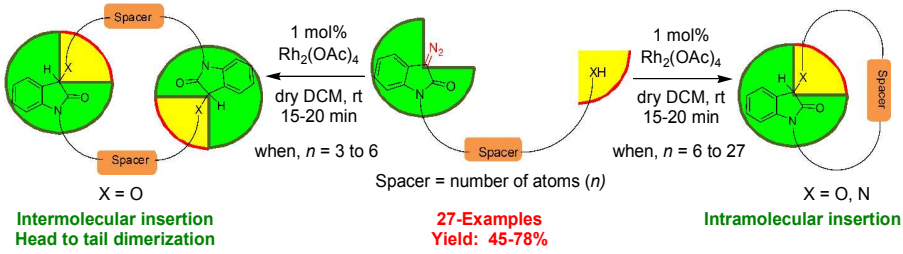
**TOC:** Synthesis of 10- to 29-membered oxaza-macrocycles *via* intramolecular O–H/N–H insertion reactions catalyzed by rhodium(II) acetate dimer is demonstrated. Synthesis of symmetric macrocycles *via* head to tail dimerization reactions is also delineated.




**Keywords:** Diazoamides / Macrocycles / Oxindoles / Rhodium(II) acetate / X–H insertion

**Abstract:** A wide variety of 10- to 29-membered oxaza-macrocycles incorporating oxindole unit were synthesized in good yield *via* rhodium(II) acetate dimer catalyzed intramolecular O–H/N–H insertion reactions. Interestingly, synthesis of $C_2$-symmetric macrocycles in moderate yield was also demonstrated *via* head to tail dimerization involving double intermolecular O-H insertion when the spacer length decreased. The synthesis of chiral macrocycles was also delineated. This study reveals the effect of spacer length on inter- or intramolecular insertion reactions with the remotely placed hydroxyl/amino group.

## Introduction

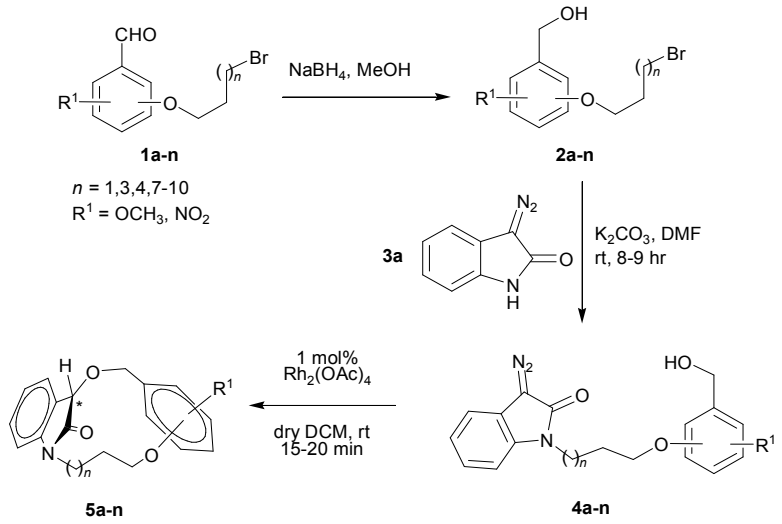
The chemistry of diazocarbonyl compounds has shown, over the years, a multitude of applications in the field of organic synthesis. Rhodium carbenoids, generated from diazocarbonyl compounds, have been useful in studying an array of reactions[1] such as cyclopropanation, insertion and ylide formation. The catalytic insertion of α-diazocarbonyl compounds into X–H

(X = C, N, O, S *etc*.) bonds was widely utilized in organic synthesis.[2] Inter- and intramolecular C–H insertion reactions[3] employing metallo-carbenoids have been investigated for the cyclic as well as acyclic compounds. However, only a limited report is available toward the synthesis of the medium-size ring systems[4] and macrocycles[5] via the metallo-carbenoid mediated C–H insertion reaction. The X–H bonds (when X = N, O, S, etc.) are generally more reactive than the corresponding C–H bond toward metallo-carbenoids. A number of examples exist in the chemical literature describing typically the intramolecular insertion of metal-stabilized carbenoid into X–H bond for the construction[6] of five/six-membered carbo- and heterocyclic ring systems. Moody[7] and co-workers have explained the formation of seven- to eight-membered-ring heterocyclic systems *via* intramolecular X–H insertion reactions. Sugimura and co-workers have reported the stereoselective synthesis of ten-membered[8] cyclic ethers *via* intramolecular O–H insertion reaction. Macrocycles were usually synthesized using high dilution techniques[9]/templates[10] and received a great deal of attention due to their large number of applications.[11] Construction of macrocycles through the metallo-carbenoid transformation[12] with diazo compounds has not received significant attention compared to the medium ring systems. In addition, synthesis of macrocycles *via* intramolecular X–H (X = N, O, S *etc*.) insertion reactions has not been noted. Especially, the oxindole moiety constitutes a key structural unit in several natural products.[13] Hence, the development of novel synthetic strategies leading to the synthesis of oxindole derivatives[14] is essential. In continuation of our interest in developing a new synthetic strategy towards the macrocyclic[15] ring systems, we herein demonstrate 10- to 29-membered oxaza-macrocycles incorporating the oxindole unit *via* intramolecular O–H/N–H insertion or intermolecular head to tail dimerization reactions using 1 mol% of rhodium(II) acetate dimer as a catalyst. The systematic study on the metallo-carbenoid mediated formation of macrocycles based on the spacer length between diazo and alcohol/amine functionality was also delineated.

**Results and discussion**

Initially, synthesis of substrates having alcohol functionality tethered on diazo compounds was planned. Towards this, O-alkylation of 2-hydroxybenzaldehyde with 1,3-dibromopropane was performed to furnish the corresponding bromobenzaldehyde **1a**. Subsequent reduction of **1a** in the presence of $NaBH_4$ in methanol afforded the corresponding alcohol[16] **2a** in very good yield.

Successive N-alkylation of 3-diazooxindole[17] **3a** with **2a** in the presence of potassium carbonate afforded the corresponding cyclic diazoamide **4a** in 88% yield.




**Scheme 1** Synthesis of dioxaza-macrocycles **5** *via* O–H insertion reaction

**Table 1** Synthesis of macrocycles **5** *via* intramolecular O–H insertion reaction

| Entry | Aldehyde | *n* | Diazo-amides **4** (yield %)[a] | Macro-cycles **5** (yield %)[a] | Macro cyclic core |
|---|---|---|---|---|---|
| 1 | 2-$OHC_6H_5CHO$ | 1 | **4a** (88) | **5a** (66) | 11 |
| 2 | 2-$OHC_6H_5CHO$ | 3 | **4b** (87) | **5b** (68) | 13 |
| 3 | 2-$OHC_6H_5CHO$ | 4 | **4c** (89) | **5c** (67) | 14 |
| 4 | 2-$OHC_6H_5CHO$ | 7 | **4d** (84) | **5d** (69) | 17 |
| 5 | 2-$OHC_6H_5CHO$ | 8 | **4e** (86) | **5e** (72) | 18 |
| 6 | 2-$OHC_6H_5CHO$ | 9 | **4f** (82) | **5f** (70) | 19 |
| 7 | 2-$OHC_6H_5CHO$ | 10 | **4g** (86) | **5g** (65) | 20 |
| 8 | Aldehyde[b] | 8 | **4h**(89) | **5h** (75) | 18 |
| 9 | Aldehyde[c] | 8 | **4i** (86) | **5i** (70) | 18 |
| 10 | 3-$OHC_6H_5CHO$ | 4 | **4j** (85) | **5j** (63) | 15 |
| 11 | 3-$OHC_6H_5CHO$ | 8 | **4k** (82) | **5k** (64) | 19 |
| 12 | 4-$OHC_6H_5CHO$ | 4 | **4l** (82) | **5l** (61) | 16 |
| 13 | 4-$OHC_6H_5CHO$ | 8 | **4m** (80) | **5m** (60) | 20 |
| 14 | 4-$OHC_6H_5CHO$ | 10 | **4n** (81) | **5n** (62) | 22 |

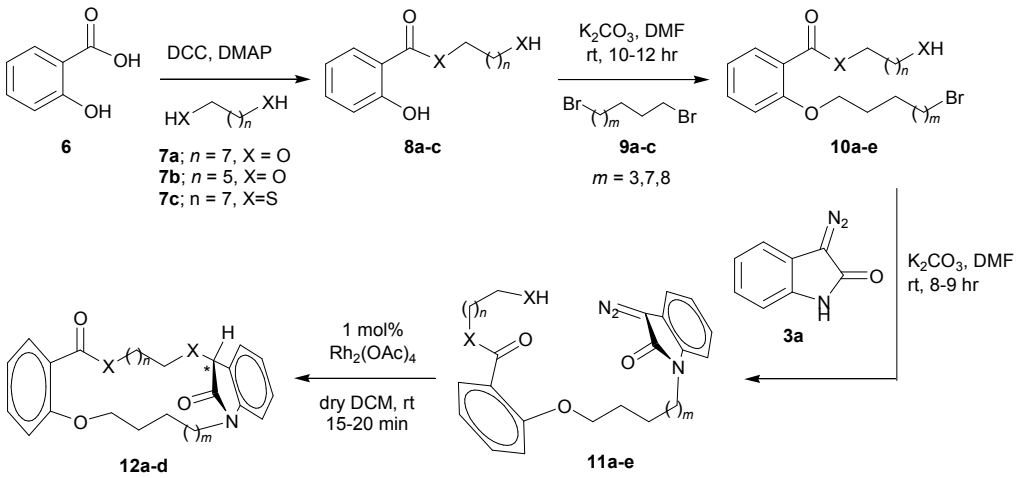
[a] Isolated yield. [b]2-OH(4-OMe)$C_6H_4CHO$. [c] 2-OH(4-$NO_2$)$C_6H_4CHO$

Our aim is to demonstrate the synthesis of macrocycles *via* intramolecular insertion reactions with remotely placed hydroxyl group of diazoamide **4**[15c] in the presence of a metal catalyst. Toward this, reaction of diazoamide **4a** in the presence of rhodium(II) acetate dimer in dry dichloromethane under argon atmosphere smoothly afforded the corresponding macrocycle **5a**

having oxindole unit in 66% yield (Scheme 1, entry 1, Table 1). Completion of the reaction took place within 20 min and no other byproducts observed based on the NMR spectrum of crude reaction mixture. The above reaction was carried out using different solvents and then optimized using dry dichloromethane at room temperature to afford macrocycle **5a**. Stimulated by this result, spacer length modifications between diazo and alcohol functionalities were planned. Thus, compounds **2** having appropriate spacer length (*n* = 1,3,4,7-10) underwent N-alkylation of 3-diazooxindole **3a** to yield the corresponding diazoamides **4b-g** in good yield. Reactions of diazoamides **4b-g** in the presence of rhodium(II) acetate dimer catalyst as described above afforded the corresponding macrocycles **5b-g** in good yield. Next, reaction of diazoamides **4h,i** having electron-donating or -withdrawing substituent was also performed under similar reaction conditions to obtain the corresponding macrocycles **5h**,**i**. Reaction of diazoamides having *m*- or *p*-substituted alcohol **4j-n** furnished the corresponding products **5j-n** in good yield.

After demonstrating the synthesis of 11- to 22-membered dioxaza-macrocycles incorporating oxindole unit *via* intramolecular O–H insertion process, the trioxaza-macrocycles having more than 22-membered systems were planned. Thus, the required substituted cyclic diazoamides **11** were assembled *via* DCC coupling of salicylic acid **6** using 1,8-octanediol **7a** to afford the corresponding hydroxyl compound[16] **8a**. Subsequent O-alkylation of compound **8a** using dibromohexane **9a** in the presence of potassium carbonate afforded the corresponding bromohydroxy compound[15] **10a** in good yield. N-alkylation of 3-diazooxindole **3a** using compound **10a** in the presence of potassium carbonate afforded alcohol tethered to diazoamide **11a** in 81% yield (Table 2). In line with the above study described in Scheme 1, the rhodium(II) catalyzed synthesis of trioxaza-macrocycles from diazoamides **11** was planned. In this direction, the substituted diazoamide **11a** in the presence of rhodium(II) acetate dimer under argon atmosphere afforded 23-membered trioxaza-macrocycle **12a** incorporating oxindole unit in 70% yield. Representatively, the structure of trioxa-macrocyclic compound **12a** was confirmed using the single crystal X-ray analysis (Figure 1).

**Table 2** Synthesis of macrocycles **12** *via* intramolecular O–H insertion reaction




| Entry | *n* | *m* | X | Diazoamides **11** (yield %)[a] | Macrocycles **12** (yield %)[a] | Size of the macrocycle |
|---|---|---|---|---|---|---|
| 1 | 7 | 3 | O | **11a** (81) | **12a** (70) | 23 |
| 2 | 7 | 9 | O | **11b** (78) | **12b** (78) | 29 |
| 3 | 5 | 9 | O | **11c** (80) | **12c** (72) | 27 |
| 4 | 7 | 7 | O | **11d** (76) | **12d** (68) | 27 |
| 5 | 7 | 3 | S | **11e** (70) | -- | -- |

[a] Isolated yield

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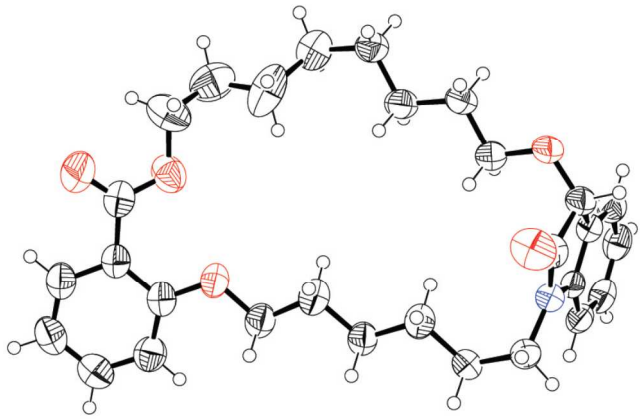


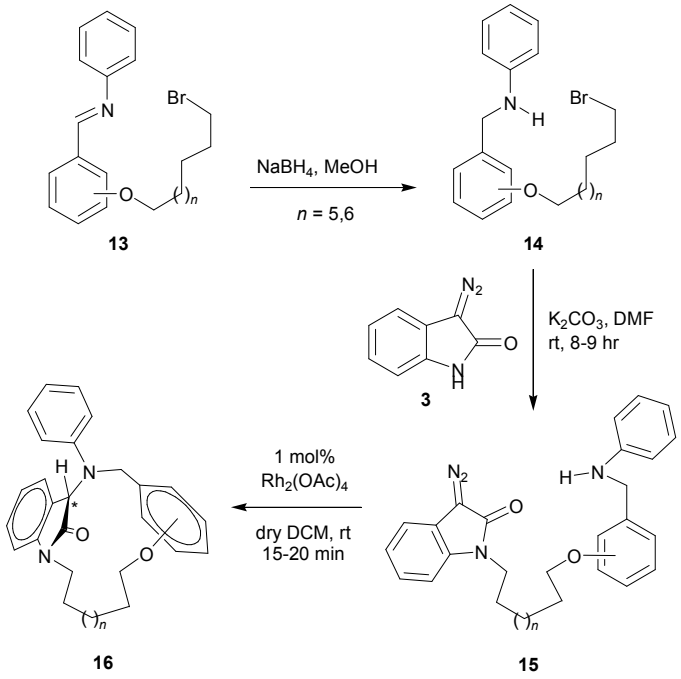
**Fig. 1** ORTEP view of macrocycle **12a**

The solid-state packing arrangement of **12a** showed the presence of a C–H···π and five intermolecular C–H···O hydrogen bonding interactions.[16] Subsequently, reactions of cyclic diazoamides **11b-d** were carried out under similar conditions by changing the spacer length (*n*,*m*) to generate the corresponding 27- and 29-membered trioxaza-macrocycles **12b-d** (Table 2). After successful demonstration of trioxaza-macrocyclic core *via* intramolecular O–H insertion

reaction, the intramolecular S–H insertion reaction was further planned. But, S–H insertion was not facile to yield a macrocycle from **11e** because of the nucleophilicity of sulphur atom might[6a,18] quench the rhodium catalyst. The diazoamide **11e** was completely recovered from the above reaction mixture.

Next, the investigation of intramolecular N–H insertion reaction was designed as there is no literature for the synthesis of macrocyles *via* N–H insertion reaction. The required staring precursor **15** was prepared from aniline and bromobenzaldehyde **1** to furnish the corresponding Schiff base **13** in good yield. Followed by the reduction of Schiff base **13a** ($n$ = 5) in the presence of $NaBH_4$ in methanol afforded the corresponding bromoamine[16] **14a** in good yield. Subsequent N-alkylation of 3-diazooxindole **3a** with **14a** afforded the corresponding amine tethered on diazoamide **15a** in 78% yield. Diazoamide **15a** in the presence of $Rh_2(OAc)_4$ dimer was carried out to furnish the corresponding 17-membered oxadiaza-macrocycle **16a** possessing oxindole unit in 68% yield (Table 3). Reactions of cyclic diazoamides **15b,c** were also carried out under similar reaction conditions to yield the corresponding 18- and 19-membered oxadiaza-macrocycles *via* intramolecular N–H insertion. A few carbon signals were missing in $^{13}C$ spectra due to the presence of symmetry in products.

**Table 3** Synthesis of macrocycles **16** *via* N–H insertion reaction



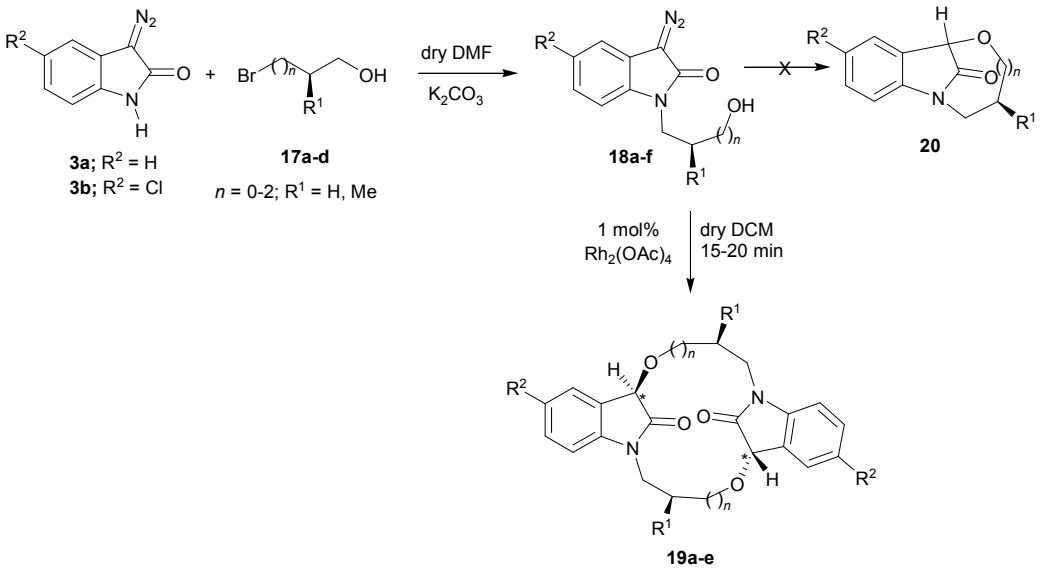
| Entry | Aldehyde | *n* | Diazoamide **15** (yield %)[a] | Macrocycle **16** (yield %)[a] | Macrocyclic core |
|---|---|---|---|---|---|
| 1 | 2-$OHC_6H_5CHO$ | 5 | **15a** (78) | **16a** (68) | 17 |
| 2 | 2-$OHC_6H_5CHO$ | 6 | **15b** (75) | **16b** (72) | 18 |
| 3 | 3-$OHC_6H_5CHO$ | 6 | **15c** (73) | **16c** (64) | 19 |

[a] Isolated yield

Based on the above study involving the synthesis of 11- to 29-membered macrocycles having oxindole unit *via* intramolecular O–H/N–H insertion reactions, our aim is next to synthesize less than 11-membered ring systems. Thus, reaction of 3-diazooxindole **3a** was reacted with 3-bromo-1-propanol (**17a**) in the presence of potassium carbonate to afford the corresponding cyclic diazoamide **18a** in 75% yield.

Subsequent reaction of diazoamide **18a** in the presence of $Rh_2(OAc)_4$ dimer in dry dichloromethane under argon atmosphere afforded an interesting dimer **19a** having two oxindole units in a diastereoselective manner (Table 4). The $^1$H NMR spectrum of **19a** revealed the presence of a singlet at $\delta$ = 4.93 ppm for oxindole (*CH) proton. $^{13}$C and DEPT-135 experiments disclosed the presence of a characteristic *CH signal at 76.1 ppm, three $CH_2$ carbons and four CH carbons (due to symmetry). The observation indicates the formation of seven-membered-ring product **20** *via* intramolecular insertion process based on $^1$H and $^{13}$C NMR spectra. However, high resolution mass spectrum clearly disclosed that the product has twice the molecular weight of **20a** as 379.1669 ($[M+H]^+$). The product structure was finally confirmed as 14-membered $C_2$-symmetric macrocycle **19a** with the additional support of single crystal X-ray analysis (Figure 2). Interstingly, the formation of macrocycle **19a** infers that the reaction underwent head to tail dimerization *via* double intermolecular O-H insertion process. The solid-state packing arrangement of **19a** showed the presence of a C–H$\cdots\pi$ and three intermolecular C–H$\cdots$O hydrogen bonding interactions.[16] In order to avoid the above dimerization process, the above reaction was performed under high dilution to yield the intramolecular O–H insertion product **20a** but in vain.

**Table 4** Synthesis of symmetric macrocycles **19** *via* head to tail dimerization process




**3a;** $R^2$ = H
**3b;** $R^2$ = Cl

**17a-d**
*n* = 0-2; $R^1$ = H, Me

**18a-f**

**20**

**19a-e**

| Entry | Bromoalcohol **17** | *n* | $R^1$ | $R^2$ | Diazoamide **18** (yield %)[a] | Macrocycle **19** (yield %)[a] | Size of the macrocycle |
|---|---|---|---|---|---|---|---|
| 1 | 3-Bromopropanol (**17a**) | 1 | H | H | **18a** (75) | **19a** (52) | 14 |
| 2 | 4-Bromobutanol (**17b**) | 2 | H | H | **18b** (73) | **19b** (50) | 16 |
| 3 | (R)-(-)-3-Bromo-2-methyl-1-propanol (**17c**) | 1 | Me | H | **18c** (65) | **19c** (45) | 14 |
| 4 | 3-Bromopropanol (**17a**) | 1 | H | Cl | **18d** (68) | **19d** (44) | 14 |
| 5 | (R)-(-)-3-Bromo-2-methyl-1-propanol (**17c**) | 1 | Me | Cl | **18e** (60) | **19e** (40) | 14 |
| 6 | 2-Bromoethanol (**17d**) | 0 | H | H | **18f** (78) | **19f**[b] | -- |

[a] Isolated yield. [b] No product formed.

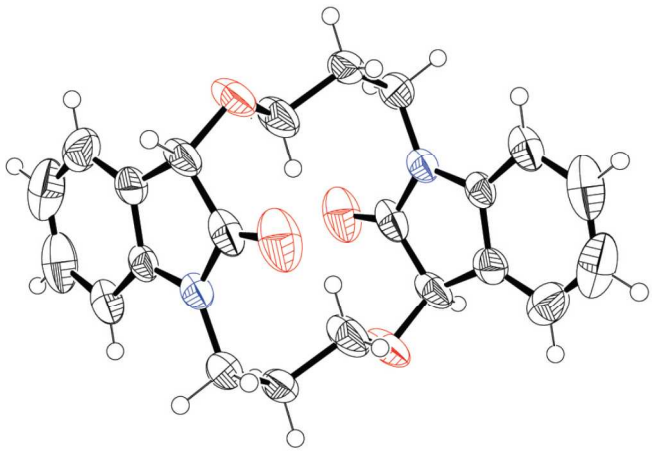
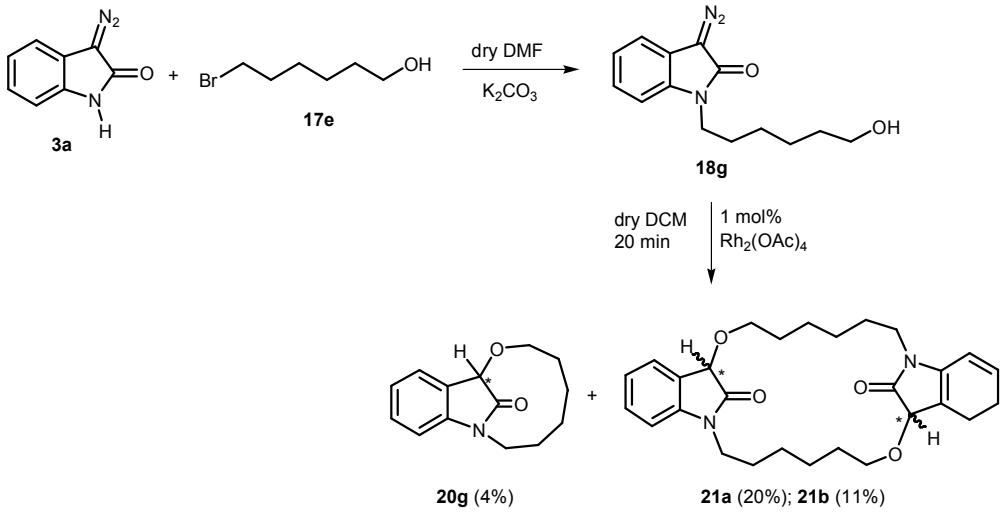


**Figure 2** ORTEP view of $C_2$-symmetric macrocycle **19a**. There are two molecules in the asymmetric unit; only one is shown for better clarity

Encouraged by this result, the above reaction was generalized under similar reaction conditions using 4-bromo-1-butanol (**17b**) instead of **17a** as the spacer to furnish the corresponding $C_2$-

symmetric macrocycle **19b** *via* intermolecular dimerization in 50% yield. Synthesis of chiral macrocycles was further planned. Thus, N-alkylation reaction of 3-diazooxindole **3a** was performed using (*R*)-(-)-3-bromo-2-methyl-1-propanol (**17c**) under similar reaction conditions to furnish the corresponding chiral diazoamide **18c** in 65% yield. Subsequent reaction of chiral diazoamide **18c** in the presence of $Rh_2(OAc)_4$ dimer under argon atmosphere furnished the chiral macrocycle **19c** in 45% yield. N-Alkylation of substituted 3-diazooxindole **3b** with 3-bromo-1-propanol (**17a**) in the presence of potassium carbonate furnished cyclic diazoamide **18d** in 68% yield. Subsequent reaction under similar reaction conditions afforded the corresponding $C_2$-symmetric macrocycle **19d** in 44% yield. The above reaction was repeated under similar reaction conditions using (R)-(-)-3-bromo-2-methyl-1-propanol (**17c**) instead of **17a** as the spacer to furnish the corresponding chiral macrocycle **19e** in 40% yield. However, reaction of substrate **18f** having a carbon less in spacer length, prepared from 2-bromoethanol, did not yield the expected product **19f** which may be due to the higher strain energy[19] involved in the product.

The above head to tail dimerization reaction yielded symmetric macrocycles having two oxindole units in a diastereoselective manner. Similar reaction of 3-diazooxindole **3a** with 6-bromo-1-hexanol (**17e**) afforded the corresponding cyclic diazoamide **18g** in 70% yield. Subsequent reaction of diazoamide **18g** in the presence of $Rh_2(OAc)_4$ dimer in dichloromethane under argon atmosphere for 20 min and subsequent chromatography purification of the reaction mixture afforded 20-membered oxaza-macrocyclic compounds **21a,b** (overall yield 32%) as a mixture of diastereomers in moderate yield and a trace amount of 10-membered oxaza-macrocyle **20g** (4%) *via* intramolecular O–H insertion reaction (Scheme 2). The diastereomers **21a,b** were present in the ratio of 58:42 and could be separable using column chromatography (Fig. 3). The $^1$H NMR spectra of **21a** (isolated yield 20%) and **21b** (isolated yield 11%) exhibited a characteristic singlet resonance at δ 4.885 and δ 4.897 for two *CH protons, respectively. The intramolecular insertion product **20g** exhibited a characteristic singlet resonance at δ 4.92 for a *CH proton. Further, these compounds exhibited consistent $^{13}$C NMR and DEPT-135 spectral data. The yield of products may vary based on the concentration of the reaction. The reaction of cyclic diazoamides **18a-e** proceeded intermolecular manner to produce the head to tail dimerization for macrocycles as a single diastereomer. However, reaction of diazoamide **18g** afforded the intramolecular product **20** as well as the intermolecular product **21** as a mixture of diastereomers.




**Scheme 2** Study of the double O–H insertion reaction of **18g**

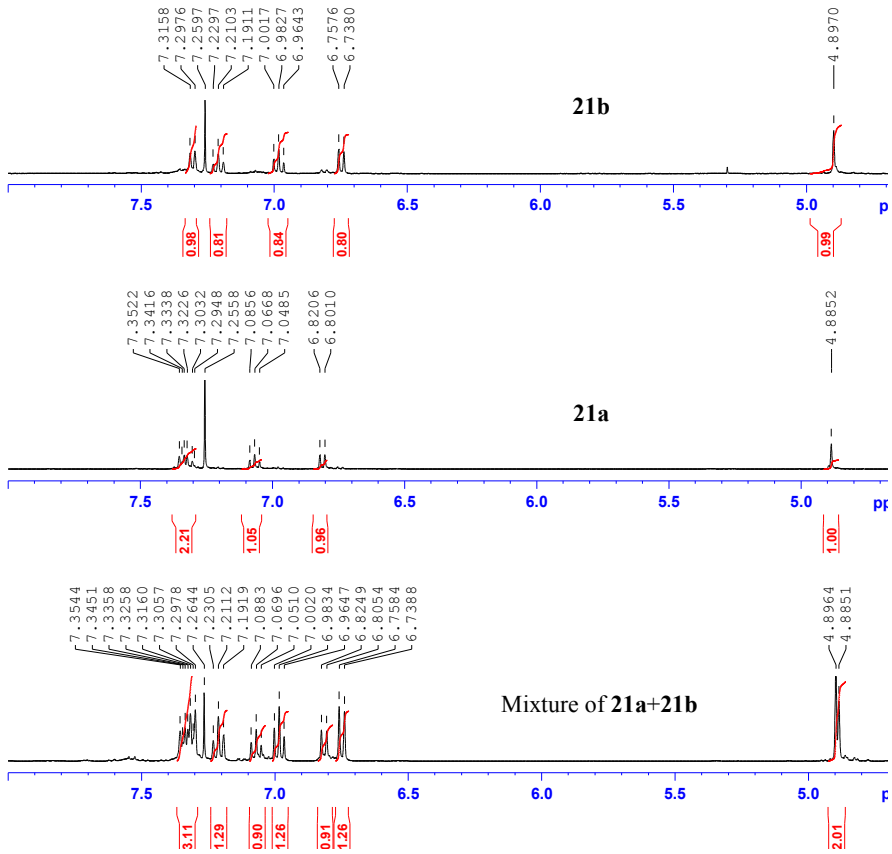



**Fig. 3** NMR spectra of diastereomers **21a,b**

## Conclusions

In conclusion, a facile, mild and convenient method to synthesize oxaza-macrocycles incorporating oxindole unit *via* intramolecular O–H/N–H insertion reactions in the presence of $Rh_2(OAc)_4$ catalyst was demonstrated. Interestingly, synthesis of $C_2$-symmetric or chiral oxaza-macrocycles in moderate yield was delineated *via* head to tail dimerization involving double intermolecular O–H insertion when the spacer length decreased. This catalytic method afforded 10- to 29-membered oxaza-macrocycles incorporating oxindole unit in good yield without using high dilution/template techniques. This study reveals the effect of spacer length based on inter- or intramolecular O–H/N–H insertion processes.

## Experimental Section

**General:** Melting points were determined on a capillary melting point apparatus and are uncorrected. IR spectra were recorded using ATR technique on a Bruker Alpha FT-IR spectrophotometer. Proton nuclear magnetic resonance ($^1$H NMR) spectra were recorded on a Bruker Avance at 400 MHz using $CDCl_3$ in ppm (δ) related to tetramethylsilane (δ = 0.00) as an internal standard and are reported as follows; chemical shift (ppm), multiplicity (br = broad, s = singlet, d = doublet, m = multiplet), coupling constant (Hz) and integration. Carbon-13 nuclear magnetic resonance ($^{13}$C NMR) spectra were recorded at 100 MHz in $CDCl_3$. Chemical shifts are reported in delta (δ) units, parts per million (ppm) relative to the center of the triplet at 77.7 ppm for $CDCl_3$. Carbon types were determined from $^{13}$C NMR and DEPT experiments. High resolution mass spectra (HRMS-ESI) were obtained on a Bruker APEX 47e FT-ICR mass spectrometer or Waters QTof-micromass spectrometer. Optical rotations were taken on a Jasco P-2000 polarimeter. All solvents were purified by distillation following standard procedure. Thin layer chromatography was performed on silica or alumina plates and components visualized under iodine/UV light at 254 nm. Column chromatography was performed on silica gel (100-200 mesh). All the reactions were conducted in oven-dried glassware under a positive pressure of argon with magnetic stirring. Reagents were added *via* syringe through septa.

**General procedure for macrocycles 5.** A solution of diazoamide **4** (150 mg, 1.0 mmol) and rhodium(II) acetate dimer (1.0 mol%) in dichloromethane (15 mL) was stirred at room temperature for 15-20 min. The progress of the reaction was monitored using TLC. After completion of the reaction, reaction mixture was concentrated under reduced pressure and

purified using column chromatography ($SiO_2$, hexane/ethyl acetate 75:25) to afford the respective macrocycles **5**.

**Synthesis of macrocycle 5a.** Colorless solid (90 mg, 66%); mp 165-167 °C; IR (neat): $\nu_{max}$ 2929, 2855, 1726, 1682, 1605, 1496, 1487, 1445, 1297, 1123, 758 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) δ = 1.76-1.80 (m, 1H), 2.30-2.41 (m, 1H), 3.47-3.51 (m, 1H), 4.06-4.18 (m, 3H), 4.31-4.38 (m, 1H), 4.48 (d, 1H, *J* = 12.8 Hz), 4.97 (s, 1H), 6.60 (d, 1H, *J* = 8 Hz), 6.81-6.86 (m, 2H), 7.05 (t, 1H, *J* = 7.6 Hz), 7.16 (td, 1H, $J_1$ = 7.2 Hz, $J_2$ = 1.6 Hz), 7.26 (dd, 1H, $J_1$ = 7.2 Hz, $J_2$ = 1.6 Hz), 7.31 (t, 1H, *J* = 7.6 Hz), 7.40 (d, 1H, $J_1$ = 7.6 Hz); $^{13}C$ NMR (100 MHz, $CDCl_3$) δ 25.16 (*C*$H_2$), 39.06 (*C*$H_2$), 62.52 (*C*$H_2$), 68.46 (*C*$H_2$), 75.57 (*C*H, observed in DEPT-90 NMR), 108.62 (=*C*H), 110.59 (=*C*H), 120.83 (=*C*H), 122.65 (=*C*H), 124.84 (*quat-C*), 125.94 (=*C*H), 125.95 (*quat-C*), 129.96 (=*C*H), 130.05 (=*C*H), 132.58 (=*C*H), 144.22 (*quat-C*), 156.51 (*quat-C*), 174.42 (*quat-C*); HRMS (ESI) Calcd for $C_{18}H_{17}NO_3$ $[M+H]^+$ 296.1287; found, 296.1292.

**Synthesis of macrocycle 5b.** Colorless solid (94 mg, 68%); mp 152-154 °C; IR (neat): $\nu_{max}$ 2922, 2853, 1713, 1613, 1603, 1494, 1468, 1360, 1256, 1167, 752 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) δ = 1.31-1.36 (m, 1H), 1.45-1.57 (m, 3H), 1.98-2.08 (m, 2H), 3.29 (ddd, 1H, $J_1$ = 14.4 Hz, $J_2$ = 4.8 Hz, $J_3$ = 1.2 Hz), 3.56-3.62 (m, 1H), 3.92 (dt, 1H, $J_1$ = 8.4 Hz, $J_2$ = 3.2 Hz), 4.36 (td, 1H, $J_1$ = 13.8 Hz, $J_2$ = 3.2 Hz), 4.38 (d, 1H, *J* = 10.4 Hz), 4.76 (s, 1H), 5.59 (d, 1H, *J* = 10.4 Hz), 6.56 (d, 1H, *J* = 8 Hz), 6.70 (d, 1H, *J* = 8 Hz), 6.76 (td, 1H, $J_1$ = 7.6 Hz, $J_2$ = 0.8 Hz), 6.86 (td, 1H, $J_1$ = 7.6 Hz, $J_2$ = 0.8 Hz), 7.10 (td, 1H, $J_1$ = 8.0 Hz, $J_2$ = 1.6 Hz), 7.15 (td, 1H, $J_1$ = 7.8 Hz, $J_2$ = 0.4 Hz), 7.21-7.26 (m, 2H); $^{13}C$ NMR (100 MHz, $CDCl_3$) δ 20.47 (*C*$H_2$), 23.41 (*C*$H_2$), 26.59 (*C*$H_2$), 36.52 (*C*$H_2$), 65.47 (*C*$H_2$), 66.06 (*C*$H_2$), 74.29 (*C*H, observed in DEPT-90 NMR), 108.89 (=*C*H), 110.41 (=*C*H), 119.75 (=*C*H), 122.50 (=*C*H), 125.64 (*quat-C*), 125.94 (=*C*H), 126.31 (*quat-C*), 129.62 (=*C*H), 131.09 (=*C*H), 143.42 (*quat-C*), 157.83 (*quat-C*), 174.09 (*quat-C*); HRMS (ESI) Calcd for $C_{20}H_{21}NO_3$ $[M+Na]^+$ 346.1419; found, 346.1410.

**Synthesis of macrocycle 5c.** Colorless solid (93 mg, 67%); mp 157–159 °C; IR (neat): $\nu_{max}$ 2927, 2856, 1710, 1613, 1488, 1467, 1466, 1367, 1263, 1163, 751 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) δ = 1.21-1.40 (m, 1H), 1.48-1.58 (m, 4H), 1.67-1.72 (m, 3H), 3.32 (dt, 1H, $J_1$ = 14.4 Hz, $J_2$ = 4.0 Hz), 3.63-3.68 (m, 1H), 3.7-4.01 (m, 1H), 4.13-4.20 (m, 1H), 4.31 (d, 1H, *J* = 10.0 Hz), 4.75 (s, 1H), 5.37 (d, 1H, *J* = 10.0 Hz), 6.68 (d, 1H, *J* = 8.0 Hz), 6.71 (d, 1H, *J* = 7.6 Hz), 6.82 (td, 1H, $J_1$ = 8.0 Hz, $J_2$ = 0.8 Hz), 6.91 (td, 1H, $J_1$ = 7.6 Hz, $J_2$ = 0.8 Hz), 7.12 (td, 1H, $J_1$ = 7.6 Hz, $J_2$ = 0.8 Hz), 7.19 (td, 1H, $J_1$ = 8.0 Hz, $J_2$ = 0.8 Hz), 7.28 (d, 1H, *J* = 7.2 Hz), 7.31 (dd, 1H,

$J_1$ = 7.6 Hz, $J_2$ = 1.6 Hz); $^{13}$C NMR (100 MHz, $CDCl_3$) δ 26.15 (*C*$H_2$), 26.61 (*C*$H_2$), 28.25 (*C*$H_2$), 29.38 (*C*$H_2$), 40.09 (*C*$H_2$), 65.74 (*C*$H_2$), 67.84 (*C*$H_2$), 75.11 (*C*H, observed in DEPT-90 NMR), 108.50 (=*C*H), 111.39 (=*C*H), 120.17 (=*C*H), 122.59 (=*C*H), 125.58 (*quat-C*), 126.32 (=*C*H), 126.44 (*quat-C*), 129.30 (=*C*H), 129.87 (=*C*H), 130.57 (=*C*H), 144.15 (*quat-C*), 157.19 (*quat-C*), 174.09 (*quat-C*); Anal. Calcd for $C_{21}H_{23}NO_3$ (337.41): C, 74.75; H, 6.87; N, 4.15. Found: C, 74.63; H, 6.83; N, 4.18.

**Synthesis of macrocycle 5d.** Colorless solid (96 mg, 69%); mp 167-169 °C; IR (neat): $\nu_{max}$ 2932, 2862, 1718, 1601, 1472, 1492, 1210, 1015, 743 $cm^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$) δ = 1.21-1.35 (m, 10H), 1.42-1.56 (m, 2H), 1.63-1.74 (m, 2H), 3.74-3.89 (m, 2H), 3.93-4.03 (m, 2H), 4.26 (d, 1H, *J* = 11.6 Hz), 4.41 (d, 1H, *J* = 11.6 Hz), 4.98 (s, 1H), 6.62 (d, 1H, *J* = 7.6 Hz), 6.85 (t, 1H, *J* = 7.6 Hz), 6.92-6.98 (m, 1H), 7.03 (dt, 1H, $J_1$ = 8.0 Hz, $J_2$ = 1.6 Hz), 7.18 (dt, 1H, $J_1$ = 7.6 Hz, $J_2$ = 2.0 Hz), 7.24-7.33 (m, 2H), 7.42-7.53 (m, 1H); $^{13}$C NMR (100 MHz, $CDCl_3$) δ 26.12 (*C*$H_2$), 26.78 (*C*$H_2$), 27.12 (*C*$H_2$), 27.49 (*C*$H_2$), 27.79 (*C*$H_2$), 28.32 (*C*$H_2$), 29.85 (*C*$H_2$), 40.12 (*C*$H_2$), 63.33 (*C*$H_2$), 66.73 (*C*$H_2$), 75.12 (*C*H, observed in DEPT-90 NMR), 108.12 (=*C*H), 109.43 (=*C*H), 119.21 (=*C*H), 120.78 (=*C*H), 123.14 (*quat-C*), 125.76 (=*C*H), 126.12 (*quat-C*), 128.04 (=*C*H), 128.86 (=*C*H), 129.12 (=*C*H), 142.92 (*quat-C*), 156.19 (*quat-C*), 175.23 (*quat-C*); HRMS (ESI) Calcd for $C_{24}H_{29}NO_3$ $[M+Na]^+$ 402.2045; found, 402.2038.

**Synthesis of macrocycle 5e.** Colorless solid (101 mg, 72%); mp 174-176 °C; IR (neat): $\nu_{max}$ 2921, 2857, 1715, 1599, 1489, 1447, 1283, 1148, 751 $cm^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$) δ = 1.19-1.30 (m, 12H), 1.60-1.63 (m, 4H), 3.36 (dt, 1H, $J_1$ = 14.0 Hz, $J_2$ = 5.6 Hz), 3.80-3.89 (m, 2H), 3.39-4.06 (m, 1H), 4.33 (d, 1H, *J* = 11.6 Hz), 4.68 (d, 1H, *J* = 11.6 Hz), 5.14 (s, 1H), 6.72 (d, 1H, *J* = 8.0 Hz), 6.77 (d, 1H, *J* = 7.6 Hz), 6.90 (td, 1H, $J_1$ = 7.6 Hz, $J_2$ = 0.8 Hz), 6.96 (td, 1H, $J_1$ = 7.6 Hz, $J_2$ = 0.8 Hz), 7.15 (td, 1H, $J_1$ = 8.0 Hz, $J_2$ = 2.0 Hz), 7.22-7.29 (m, 2H), 7.50 (dd, 1H, $J_1$ = 7.4 Hz, $J_2$ = 1.6 Hz); $^{13}$C NMR (100 MHz, $CDCl_3$) δ 25.09 (*C*$H_2$), 25.81 (*C*$H_2$), 26.56 (*C*$H_2$), 26.58 (*C*$H_2$), 26.71 (*C*$H_2$), 26.96 (*C*$H_2$), 27.02 (*C*$H_2$), 28.60 (*C*$H_2$), 39.47 (*C*$H_2$), 62.88 (*C*$H_2$), 67.90 (*C*$H_2$), 75.70 (*C*H, observed in DEPT-90 NMR), 108.78 (=*C*H), 110.75 (=*C*H), 120.22 (=*C*H), 122.62 (=*C*H), 124.82 (*quat-C*), 125.37 (=*C*H), 126.47 (*quat-C*), 128.46 (=*C*H), 128.61 (=*C*H), 129.76 (=*C*H), 143.80 (*quat-C*), 156.29 (*quat-C*), 174.19 (*quat-C*); HRMS (ESI) Calcd for $C_{25}H_{31}NO_3$ $[M+Na]^+$ 416.2202; found, 416.2211.

**Synthesis of macrocycle 5f.** Colorless solid (98 mg, 70%); mp 170–172 °C; IR (neat): $\nu_{max}$ 2942, 2892, 1765, 1623, 1413, 1446, 1219, 1067, 912, 738 $cm^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$) δ

= 1.25-1.39 (m, 12H), 1.40-1.49 (m, 4H), 1.59-1.64 (m, 2H), 3.65-3.72 (m, 2H), 3.84-3.92 (m, 2H), 4.06 (d, 1H, $J$ = 11.6 Hz), 4.12 (d, 1H, $J$ = 11.6 Hz), 4.72 (s, 1H), 6.68 (d, 1H, $J$ = 7.2 Hz), 6.79 (t, 1H, $J$ = 8.0 Hz), 6.85-6.92 (m, 1H), 7.13 (d, 1H, $J$ = 8.0 Hz), 7.22 (dt, 1H, $J_1$ = 7. 6 Hz, $J_2$ = 2.0 Hz), 7.27-7.36 (m, 2H), 7.40-7.49 (m, 1H); $^{13}$C NMR (100 MHz, $CDCl_3$) δ 26.09 (*C*$H_2$), 26.46 (*C*$H_2$), 26.79 (*C*$H_2$), 27.23 (*C*$H_2$), 27.56 (*C*$H_2$), 27.89 (*C*$H_2$), 28.12 (*C*$H_2$), 28.45 (*C*$H_2$), 29.63 (*C*$H_2$), 39.78 (*C*$H_2$), 64.12 (*C*$H_2$), 67.56 (*C*$H_2$), 74.38 (*C*H, observed in DEPT-90 NMR), 107.67 (=*C*H), 109.23 (=*C*H), 118.91 (=*C*H), 119.18 (=*C*H), 122.76 (*quat-C*), 124.17 (=*C*H), 125.67 (*quat-C*), 127.67 (=*C*H), 128.12 (=*C*H), 129.89 (=*C*H), 140.24 (*quat-C*), 155.34 (*quat-C*), 176.12 (*quat-C*); Anal. Calcd for $C_{26}H_{33}NO_3$ (407.55): C, 76.62; H, 8.16; N, 3.44. Found: C, 76.51; H, 8.14; N, 3.41.

**Synthesis of macrocycle 5g.** Colorless solid (91 mg, 65%); mp 162-164 °C; IR (neat): $\nu_{max}$ 2922, 2853, 1713, 1614, 1489, 1464, 1455, 1235, 1105, 747 cm$^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$) δ = 1.18-1.38 (m, 16H), 1.64-1.69 (m, 4H), 3.57-3.62 (m, 1H), 3.77-3.81 (m, 1H), 3.87-3.90 (m, 2H), 4.64 (d, 1H, $J$ = 11.6 Hz), 4.80 (d, 1H, $J$ = 11.6 Hz), 5.00 (s, 1H), 6.72-6.77 (m, 2H), 6.89 (t, 1H, $J$ = 7.6 Hz), 6.95 (t, 1H, $J$ = 7.6 Hz), 7.15-7.26 (m, 3H), 7.40 (dd, 1H, $J_1$ = 7.4 Hz, $J_2$ = 1.2 Hz); $^{13}$C NMR (100 MHz, $CDCl_3$) δ 25.49 (*C*$H_2$), 26.07 (*C*$H_2$), 26.15 (*C*$H_2$), 27.04 (*C*$H_2$), 27.14 (*C*$H_2$), 27.23 (*C*$H_2$), 27.38 (*C*$H_2$), 27.82 (*C*$H_2$), 28.35 (*C*$H_2$), 29.21 (*C*$H_2$), 39.42 (*C*$H_2$), 64.57 (*C*$H_2$), 68.20 (*C*$H_2$), 75.43 (*C*H, observed in DEPT-90 NMR), 108.52 (=*C*H), 111.16 (=*C*H), 120.27 (=*C*H), 122.50 (=*C*H), 125.37 (*quat-C*), 125.47 (=*C*H), 126.54 (*quat-C*), 128.79 (=*C*H), 129.26 (=*C*H), 129.68 (=*C*H), 143.78 (*quat-C*), 156.73 (*quat-C*), 174.45 (*quat-C*); HRMS (ESI) Calcd for $C_{27}H_{35}NO_3$ $[M+H]^+$ 422.2695; found, 422.2703.

**Synthesis of macrocycle 5h.** Colorless solid (105 mg, 75%); mp 178-180 °C; IR (neat): $\nu_{max}$ 2927, 2855, 1718, 1612, 1589, 1508, 1488, 1466, 1287, 1162, 732 cm$^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$) δ = 1.19-1.32 (m, 12H), 1.59-1.68 (m, 4H), 3.37-3.42 (m, 1H), 3.72 (s, 3H, OC$H_3$), 3.77-3.82 (m, 1H), 3.85-3.89 (m, 1H), 3.96-4.03 (m, 1H), 4.35 (d, 1H, $J$ = 11.2 Hz), 4.64 (d, 1H, $J$ = 11.2 Hz), 5.08 (s, 1H), 6.32 (d, 1H, $J$ = 2.0 Hz), 6.42 (dd, 1H, $J_1$ = 8.4 Hz, $J_2$ = 2.4 Hz), 6.76 (d, 1H, $J$ = 7.6 Hz), 6.96 (t, 1H, $J$ = 7.6 Hz), 7.19-7.27 (m, 2H), 7.35 (d, 1H, $J$ = 8.4 Hz); $^{13}$C NMR (100 MHz, $CDCl_3$) δ 25.18 (*C*$H_2$), 25.62 (*C*$H_2$), 26.42 (*C*$H_2$), 26.67 (*C*$H_2$), 26.79 (*C*$H_2$), 26.97 (*C*$H_2$), 27.08 (*C*$H_2$), 28.55 (*C*$H_2$), 39.31 (*C*$H_2$), 55.35 (O*C*$H_3$), 63.30 (*C*$H_2$), 68.06 (*C*$H_2$), 75.54 (*C*H, observed in DEPT-90 NMR), 98.85 (=*C*H), 104.08 (=*C*H), 108.71 (=*C*H), 119.02 (*quat-C*), 122.54 (=*C*H), 125.11 (*quat-C*), 125.35 (=*C*H), 129.66 (=*C*H), 130.07 (=*C*H), 143.75 (*quat-C*),

157.73 (*quat-C*), 160.46 (*quat-C*), 174.39 (*quat-C*); HRMS (ESI) Calcd for $C_{26}H_{33}NO_4$ $[M+H]^+$ 424.2488; found, 424.2495.

**Synthesis of macrocycle 5i.** Colorless solid (99 mg, 70%); mp 175-177 °C; IR (neat): $\nu_{max}$ 2924, 2853, 1714, 1610, 1590, 1510, 1485, 1336, 1263, 1108, 750 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) δ = 1.24-1.32 (m, 11H), 1.59-1.71 (m, 5H), 3.34 (td, 1H, $J_1$ = 14 Hz, $J_2$ = 6 Hz), 3.92-3.97 (m, 2H), 4.05-4.13 (m, 1H), 4.26 (d, 1H, $J$ = 12.8 Hz), 4.58 (d, 1H, $J$ = 12.8 Hz), 5.21 (s, 1H), 6.76 (d, 1H, $J$ = 9.2 Hz), 6.81 (d, 1H, $J$ = 8.0 Hz), 7.01 (t, 1H, $J$ = 7.6 Hz), 7.28 (t, 1H, $J$ = 8.0 Hz), 7.36 (d, 1H, $J$ = 7.2 Hz), 8.08 (dd, 1H, $J_1$ = 8.8 Hz, $J_2$ = 2.8 Hz), 8.47 (d, 1H, $J$ = 2.8 Hz); $^{13}C$ NMR (100 MHz, $CDCl_3$) δ 23.81 ($CH_2$), 25.12 ($CH_2$), 25.41 ($CH_2$), 25.52 ($CH_2$), 25.65 ($CH_2$), 25.81 ($CH_2$), 26.02 ($CH_2$), 27.24 ($CH_2$), 38.70 ($CH_2$), 60.32 ($CH_2$), 68.10 ($CH_2$), 74.69 (*C*H, observed in DEPT-90 NMR), 107.98 (=*C*H), 109.11 (=*C*H), 121.87 (=*C*H), 122.86 (=*C*H), 123.02 (*quat-C*), 123.75 (=*C*H), 124.41 (*quat-C*), 126.80 (=*C*H), 129.12 (=*C*H), 140.32 (*quat-C*), 142.86 (*quat-C*), 159.83 (*quat-C*), 172.56 (*quat-C*); HRMS (ESI) Calcd for $C_{25}H_{30}N_2O_5$ $[M+H]^+$ 439.2233; found, 439.2237.

**Synthesis of macrocycle 5j.** Colorless solid (87 mg, 63%); mp 170-172 °C; IR (neat): $\nu_{max}$ 2926, 2855, 1714, 1611, 1488, 1467, 1367, 1263, 1163, 731 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) δ = 1.35-1.55 (m, 4H), 1.61-1.68 (m, 4H), 3.26 (dt, 1H, $J_1$ = 14 Hz, $J_2$ = 4.4 Hz), 3.97-4.15 (m, 3H), 4.72 (d, 1H, $J$ = 11.6 Hz), 4.80 (s, 1H), 5.38 (d, 1H, $J$ = 11.6 Hz), 6.68 (dd, 1H, $J_1$ = 8.2 Hz, $J_2$ = 2.0 Hz), 6.73 (d, 1H, $J$ = 8.0 Hz), 6.78-6.81 (m, 2H), 6.99 (td, 1H, $J_1$ = 7.2 Hz, $J_2$ = 0.8 Hz), 7.10 (t, 1H, $J$ = 7.6 Hz), 7.24 (td, 1H, $J_1$ = 7.2 Hz, $J_2$ = 0.8 Hz), 7.36 (d, 1H, $J$ = 7.6 Hz); $^{13}C$ NMR (100 MHz, $CDCl_3$) δ 24.70 ($CH_2$), 26.55 ($CH_2$), 26.92 ($CH_2$), 27.17 ($CH_2$), 39.05 ($CH_2$), 66.78 ($CH_2$), 70.45 ($CH_2$), 74.41 (*C*H, observed in DEPT-90 NMR), 108.83 (=*C*H), 113.73 (=*C*H), 116.24 (=*C*H), 120.15 (=*C*H), 122.72 (=*C*H), 125.14 (*quat-C*), 126.22 (=*C*H), 129.25 (=*C*H), 130.06 (=*C*H), 139.85 *quat-C*), 143.89 (*quat-C*), 157.93 (*quat-C*), 175.05 (*quat-C*); HRMS (ESI) Calcd for $C_{21}H_{23}NO_3$ $[M+Na]^+$ 360.1576; found, 360.1584.

**Synthesis of macrocycle 5k.** Colorless solid (90 mg, 64%); mp 159-161 °C; IR (neat): $\nu_{max}$ 2922, 2856, 1709, 1613, 1601, 1488, 1465, 1454, 1240, 1074, 752 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) δ = 1.21-1.34 (m, 10H), 1.34-1.37 (m, 2H), 1.57-1.65 (m, 4H), 3.44-3.50 (m, 1H), 3.80-3.87 (m, 1H), 3.97 (dt, 2H, $J_1$ = 6.8 Hz, $J_2$ = 1.2 Hz), 4.75 (d, 1H, $J$ = 11.2 Hz), 4.79 (s, 1H), 5.02 (d, 1H, $J$ = 11.2 Hz), 6.72 (d, 1H, $J$ = 7.6 Hz), 6.75 (dd, 1H, $J_1$ = 2.0 Hz, $J_2$ = 0.8 Hz), 6.90 (d, 1H, $J$ = 7.6 Hz), 6.94-6.98 (m, 2H), 7.16 (d, 1H, $J$ = 8.0 Hz), 7.19-7.23 (m, 1H), 7.29 (d, 1H, $J$ =

7.6 Hz); $^{13}$C NMR (100 MHz, $CDCl_3$) δ 24.45 (*C*$H_2$), 26.06 (*C*$H_2$), 27.02 (*C*$H_2$), 27.70 (*C*$H_2$), 27.94 (*C*$H_2$), 28.49 (*C*$H_2$), 28.69 (*C*$H_2$), 39.14 (*C*$H_2$), 68.16 (*C*$H_2$), 71.33 (*C*$H_2$), 74.13 (C*H*, observed in DEPT-90 NMR), 108.63 (=*C*H), 115.03 (=*C*H), 115.87 (=*C*H), 120.39 (=*C*H), 122.56 (=*C*H), 125.61 (=*C*H), 125.66 (*quat-C*), 129.46 (=*C*H), 129.79 (=*C*H), 138.84 (*quat-C*), 143.69 (*quat-C*), 159.01 (*quat-C*), 174.90 (*quat-C*); Anal. Calcd for $C_{25}H_{31}NO_3$ (393.52): C, 76.30; H, 7.94; N, 3.56. Found: C, 76.43; H, 7.90; N, 3.59.

**Synthesis of macrocycle 5l.** Colorless solid (84 mg, 61%,); mp 161-163 °C; IR (neat): $\nu_{max}$ 2926, 2855, 1718, 1611, 1605, 1512, 1488, 1467, 1366, 1264, 1164, 731 $cm^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$) δ = 1.32-1.41 (m, 4H), 1.57-1.65 (m, 4H), 3.45-3.55 (m, 1H), 3.78 (t, 3H, *J* = 6.4 Hz), 4.53 (d, 1H, *J* = 6 Hz), 4.59 (s, 1H), 4.81 (d, 1H, *J* = 6 Hz), 6.07-6.64 (m, 2H), 6.73 (d, 1H, *J* = 8 Hz), 6.95-7.00 (m, 1H), 7.11 (t, 2H, $J_1$ = 7.6 Hz), 7.20-7.27 (m, 2H); $^{13}$C NMR (100 MHz, $CDCl_3$) δ 25.51 (*C*$H_2$), 26.31 (*C*$H_2$), 27.17 (*C*$H_2$), 28.59 (*C*$H_2$), 39.56 (*C*$H_2$), 67.39 (*C*$H_2$), 69.80 (*C*$H_2$), 74.08 (*C*H, observed in DEPT-90 NMR), 108.59 (=*C*H), 114.46 (=*C*H), 122.62 (=*C*H), 125.30 (*quat-C*), 125.39 (=*C*H), 125.51 (*quat-C*), 125.55 (=*C*H), 129.16 (=*C*H), 129.76 (=*C*H), 130.00 (=*C*H), 143.70 (*quat-C*), 158.71 (*quat-C*), 174.84 (*quat-C*); HRMS (ESI) Calcd for $C_{21}H_{23}NO_3$ $[M+Na]^+$ 360.1576; found, 360.1568.

**Synthesis of macrocycle 5m.** Colorless solid (84 mg, 60%); mp 163-165 °C; IR (neat): $\nu_{max}$ 2927, 2855, 1720, 1611, 1510, 1488, 1467, 1263, 1173, 733 $cm^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$) δ = 1.10-1.23 (m, 12H), 1.25-1.38 (m, 2H), 1.62-1.65 (m, 2H), 3.10-3.14 (m, 1H), 3.25-3.32 (m, 1H), 3.96 (t, 2H, *J* = 5.6 Hz), 4.50 (d, 1H, *J* = 12.0 Hz), 4.77 (d, 1H, *J* = 12.0 Hz), 4.85 (s, 1H), 6.62 (d, 1H, *J* = 7.6 Hz), 6.65-6.69 (m, 2H), 6.92 (d, 2H, *J* = 8.8 Hz), 7.03 (t, 1H, *J* = 7.6 Hz), 7.25 (t, 1H, *J* = 7.6 Hz), 7.38 (d, 1H, *J* = 7.2 Hz); $^{13}$C NMR (100 MHz, $CDCl_3$) δ 23.75 (*C*$H_2$), 26.04 (*C*$H_2$), 26.39 (*C*$H_2$), 26.86 (*C*$H_2$), 27.05 (*C*$H_2$), 27.52 (*C*$H_2$), 27.63 (*C*$H_2$), 27.87 (*C*$H_2$), 39.80 (*C*$H_2$), 66.49 (*C*$H_2$), 69.31 (*C*$H_2$), 73.85 (C*H*, observed in DEPT-90 NMR), 108.68 (=*C*H), 114.41 (=*C*H), 122.13 (=*C*H), 124.02 (*quat-C*), 125.85 (=*C*H), 128.51 (*quat-C*), 129.84 (=*C*H), 131.03 (=*C*H), 143.94 (*quat-C*), 158.77 (*quat-C*), 174.46 (*quat-C*); HRMS (ESI) Calcd for $C_{25}H_{31}NO_3$ $[M+Na]^+$ 416.2202; found, 416.2211.

**Synthesis of macrocycle 5n.** Colorless solid (87 mg, 62%); mp 181-183 °C; IR (neat): $\nu_{max}$ 2926, 2854, 1715, 1610, 1510, 1486, 1487, 1336, 1299, 1093, 1016, 750 $cm^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$) δ = 1.14-1.35 (m, 12H), 1.45-1.59 (m, 8H), 3.33-3.36 (m, 1H), 3.69-3.74 (m, 1H), 3.98-4.04 (m, 2H), 4.57 (d, 1H, *J* = 11.2 Hz), 4.81 (s, 1H), 4.88 (d, 1H, *J* = 11.2 Hz), 6.69 (d, 1H,

*J* = 8.0 Hz), 6.73-6.75 (m, 2H), 7.00 (t, 1H, *J* = 7.2 Hz), 7.15 (d, 2H, *J* = 8.4 Hz), 7.23 (t, 1H, *J* = 7.2 Hz), 7.36 (d, 1H, *J* = 7.2 Hz); $^{13}$C NMR (100 MHz, $CDCl_3$) δ 25.28 (*C*$H_2$), 26.17 (*C*$H_2$), 26.19 (*C*$H_2$), 27.24 (*C*$H_2$), 27.34 (*C*$H_2$), 27.63 (*C*$H_2$), 27.78 (*C*$H_2$), 28.12 (*C*$H_2$), 28.45 (*C*$H_2$), 29.15 (*C*$H_2$), 39.22 (*C*$H_2$), 64.23 (*C*$H_2$), 68.74 (*C*$H_2$), 75.11 (*C*H, observed in DEPT-90 NMR), 108.32 (=*C*H), 111.54 (=*C*H), 120.05 (=*C*H), 122.32 (=*C*H), 125.51 (*quat-C*), 125.87 (=*C*H), 126.24 (*quat-C*), 127.76 (=*C*H), 128.16 (=*C*H), 129.28 (=*C*H), 145.18 (*quat-C*), 156.33 (*quat-C*), 175.15 (*quat-C*); HRMS (ESI) Calcd for $C_{27}H_{35}NO_3$ $[M+Na]^+$ 444.2515; found, 444.2509.

**General procedure for diazoamides 11**

To an oven-dried flask, a solution containing 3-diazooxindole **3a** (200 mg, 1.25 mmol) and potassium carbonate (434 mg, 3.14 mmol) in dry DMF was taken under argon atmosphere. To this reaction mixture, a solution of appropriate aliphatic bromoalcohol **10** (1.35 mmol) in dry DMF was slowly added over a period of 30 min and then a catalytic amount of tetrabutylammonium iodide. The progress of the reaction was monitored using TLC. The mixture was extracted with dichloromethane (3×25 mL) and the combined organic layers were washed with water (3×25 mL), brine (2×25 mL) and dried (anhydrous $Na_2SO_4$). The solvent was removed under reduced pressure and the resulting residue purified using column chromatography ($SiO_2$, hexane/ethyl acetate 80:20) to afford the respective diazoamides **11**.

**Synthesis of diazoamide 11a.** Red viscous liquid (516 mg, 81%); IR (neat): $\nu_{max}$ 3445, 2930, 2858, 2096, 1721, 1605, 1460, 1359, 1300, 1246, 1084, 753 cm$^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$) δ = 1.71-1.27 (m, 3H), 1.33-1.38 (m, 3H), 1.46-1.49 (m, 4H), 1.63-1.69 (m, 5H), 1.73-1.98 (m, 3H), 3.56 (t, 2H, *J* = 6.4 Hz), 3.77 (t, 2H, *J* = 7.2 Hz), 3.94 (t, 2H, *J* = 6.4 Hz), 4.05 (q, 2H, *J* = 7.6 Hz), 4.18 (t, 2H, *J* = 7.2 Hz), 6.84-6.90 (m, 3H), 7.01 (td, 1H, $J_1$ = 7.8 Hz, $J_2$ = 0.8 Hz), 7.09-7.14 (m, 2H), 7.33-7.35 (m, 1H), 7.69 (dd, 1H, $J_1$ = 7.6 Hz, $J_2$ = 2.0 Hz); $^{13}$C NMR (100 MHz, $CDCl_3$) δ 25.70 (*C*$H_2$), 26.00 (*C*$H_2$), 26.60 (*C*$H_2$), 28.04 (*C*$H_2$), 28.41 (*C*$H_2$), 28.75 (*C*$H_2$), 29.08 (*C*$H_2$), 29.26 (*C*$H_2$), 29.32 (*C*$H_2$), 32.73 (*C*$H_2$), 40.65 (*C*$H_2$), 41.39 (*C*$H_2$), 62.90 (*C*$H_2$), 64.93 (*C*$H_2$), 68.61 (*C*$H_2$), 108.95 (=*C*H), 113.11 (=*C*H), 116.86 (*quat-C*), 118.35 (=*C*H), 120.02 (=*C*H), 120.82 (*quat-C*), 121.95 (=*C*H), 125.42 (=*C*H), 131.53 (=*C*H), 133.19 (=*C*H), 133.82 (*quat-C*), 158.45 (*quat-C*), 166.71 (*quat-C*), 166.74 (*quat-C*); Anal. Calcd for $C_{29}H_{37}N_3O_5$ (507.62): C, 68.62; H, 7.35; N, 8.28. Found: C, 68.71; H, 7.30; N, 8.21.

**Synthesis of diazoamide 11b.** Red viscous liquid (580 mg, 78%); IR (neat): $\nu_{max}$ 3445, 2924, 2854, 2094, 1688, 1604, 1460, 1300, 1246, 1134, 1082, 751 cm$^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$) δ

= 1.26 (br, m, 9H), 1.35 (br, m, 9H), 1.42-1.47 (m, 4H), 1.55-1.58 (m, 2H), 1.66-1.83 (m, 8H), 3.63 (t, 2H, $J$ = 6.8 Hz), 3.81 (t, 1H, $J$ = 7.6 Hz), 4.01 (t, 2H, $J$ = 6.4 Hz), 4.28 (t, 2H, $J$ = 6.4 Hz), 6.92-6.97 (m, 3H), 7.07 (t, 1H, $J$ = 7.6 Hz), 7.16-7.21 (m, 2H), 7.42 (td, 1H, $J_1$ = 7.6 Hz, $J_2$ = 1.6 Hz), 7.76 (dd, 1H, $J_1$ = 8.0 Hz, $J_2$ = 1.6 Hz); $^{13}$C NMR (100 MHz, $CDCl_3$) δ 25.73 (*C*$H_2$), 26.01 (*C*$H_2$), 26.89 (*C*$H_2$), 28.07 (*C*$H_2$), 28.76 (*C*$H_2$), 29.25 (*C*$H_2$), 29.30 (*C*$H_2$), 29.35 (*C*$H_2$), 29.41 (*C*$H_2$), 29.50 (*C*$H_2$), 29.58 (*C*$H_2$), 32.78 (*C*$H_2$), 40.79 (*C*$H_2$), 62.97 (*C*$H_2$), 64.96 (*C*$H_2$), 68.90 (*C*$H_2$), 108.92 (=*C*H), 113.11 (=*C*H), 116.89 (*quat-C*), 118.32 (=*C*H), 119.94 (=*C*H), 120.89 (*quat-C*), 121.86 (=*C*H), 125.37 (=*C*H), 131.52 (=*C*H), 133.13 (=*C*H), 133.94 (*quat-C*), 158.53 (*quat-C*), 166.76 (*quat-C*), 166.86 (*quat-C*); Anal. Calcd for $C_{35}H_{49}N_3O_5$ (591.78): C, 71.04; H, 8.35; N, 7.10. Found: C, 71.19; H, 8.40; N, 7.16.

**Synthesis of diazoamide 11c.** Red viscous liquid (566 mg, 80%); IR (neat): $\nu_{max}$ 3449, 2925, 2855, 2092, 1683, 1694, 1603, 1460, 1300, 1245, 1135, 1080, 749 cm$^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$) δ = 1.26-1.33 (m, 14H), 1.39-1.50 (m, 6H), 1.55-1.62 (m, 2H), 1.67-1.85 (m, 6H), 2.04 (br, s, 1H), 3.63 (t, 2H, $J$ = 6.4 Hz), 3.80 (t, 2H, $J$ = 7.6 Hz), 4.01 (t, 2H, $J$ = 6.4 Hz), 4.29 (t, 2H, $J$ = 7.2 Hz), 6.92-6.96 (m, 3H), 7.06 (t, 1H, $J$ = 7.6 Hz), 7.18 (t, 2H, $J$ = 7.6 Hz), 7.41 (td, 1H, $J_1$ = 8.0 Hz, $J_2$ = 1.6 Hz), 7.76 (dd, 1H, $J_1$ = 8.0 Hz, $J_2$ = 2.0 Hz); $^{13}$C NMR (100 MHz, $CDCl_3$) δ 25.49 (*C*$H_2$), 25.88 (*C*$H_2$), 26.00 (*C*$H_2$), 26.86 (*C*$H_2$), 28.06 (*C*$H_2$), 28.77 (*C*$H_2$), 29.23 (*C*$H_2$), 29.28 (*C*$H_2$), 29.39 (*C*$H_2$), 29.48 (*C*$H_2$), 29.56 (*C*$H_2$), 32.66 (*C*$H_2$), 40.77 (*C*$H_2$), 62.71 (*C*$H_2$), 64.82 (*C*$H_2$), 68.88 (*C*$H_2$), 108.94 (=*C*H), 113.10 (=*C*H), 116.86 (*quat-C*), 118.33 (=*C*H), 119.94 (=*C*H), 120.81 (*quat-C*), 121.88 (=*C*H), 125.38 (=*C*H), 131.51 (=*C*H), 133.17 (=*C*H), 133.89 (*quat-C*), 158.53 (*quat-C*), 166.78 (*quat-C*), 166.84 (*quat-C*); Anal. Calcd for $C_{33}H_{45}N_3O_5$ (563.73): C, 70.31; H, 8.05; N, 7.45. Found: C, 70.44; H, 8.09; N, 7.51.

**Synthesis of diazoamide 11d.** Red viscous liquid (538 mg, 76%); IR (neat): $\nu_{max}$ 3439, 2934, 2823, 2091, 1673, 1612, 1423, 1315, 1223, 1146, 1039, 746 cm$^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$) δ = 1.21-1.36 (m, 16H), 1.45-1.49 (m, 6H), 1.56-1.68 (m, 6H), 3.58 (t, 2H, $J$ = 7.2 Hz), 3.78 (t, 2H, $J$ = 7.6 Hz), 3.96 (t, 2H, $J$ = 6.8 Hz), 4.53 (t, 2H, $J$ = 7.2 Hz), 6.78-6.83 (m, 2H), 6.94 (t, 2H, $J$ = 7.2 Hz), 7.02-7.12 (m, 2H), 7.25 (d, 1H, $J$ = 7.6 Hz), 7.41 (d, 1H, $J$ = 7.2 Hz); $^{13}$C NMR (100 MHz, $CDCl_3$) δ 24.45 (*C*$H_2$), 25.45 (*C*$H_2$), 26.12 (*C*$H_2$), 27.23 (*C*$H_2$), 28.12 (*C*$H_2$), 28.76 (*C*$H_2$), 29.46 (*C*$H_2$), 29.54 (*C*$H_2$), 29.78 (*C*$H_2$), 32.29 (*C*$H_2$), 41.23 (*C*$H_2$), 62.97 (*C*$H_2$), 65.12 (*C*$H_2$), 66.83 (*C*$H_2$), 109.48 (=*C*H), 112.76 (=*C*H), 117.59 (*quat-C*), 118.31 (=*C*H), 119.90 (=*C*H), 121.23 (*quat-C*), 121.75 (=*C*H), 126.49 (=*C*H), 132.12 (=*C*H), 134.34 (=*C*H), 134.74 (*quat-C*),

159.12 (*quat-C*), 167.46 (*quat-C*), 167.76 (*quat-C*); Anal. Calcd for $C_{33}H_{45}N_3O_5$ (563.73): C, 70.31; H, 8.05; N, 7.45. Found: C, 70.19; H, 8.00; N, 7.38.

**General procedure for synthesis of macrocycles 12.** A solution of diazoamide **11** (150 mg, 1.0 mmol) and rhodium(II) acetate dimer (1.0 mol%) in dichloromethane (15 mL) was stirred at room temperature for 15-20 min. The progress of the reaction was monitored using TLC. After completion of the reaction, reaction mixture was concentrated under reduced pressure and purified using column chromatography ($SiO_2$, hexane/ethyl acetate 75:25) to afford the respective macrocycle **12**.

**Synthesis of macrocycle 12a.** Colorless solid (99 mg, 70%); mp 198-200 °C; IR (neat): $\nu_{max}$ 2923, 2852, 1713, 1694, 1598, 1449, 1352, 1303, 1230, 1048, 757 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) δ = 1.13-1.32 (m, 5H), 1.33-1.38 (m, 6H), 1.52-1.62 (m, 6H), 1.68-1.73 (m, 3H), 3.25-3.34 (m, 2H), 3.45-3.51 (m, 1H), 3.85-3.93 (m, 2H), 4.05-4.12 (m, 1H), 4.16-4.24 (m, 2H), 4.86 (s, 1H), 6.76 (d, 1H, $J$ = 7.6 Hz), 6.83 (d, 1H, $J$ = 8.4 Hz), 6.87 (td, 1H, $J_1$ = 7.6 Hz, $J_2$ = 1.6 Hz), 7.01 (t, 1H, $J$ = 7.6 Hz), 7.25 (t, 1H, $J$ = 7.6 Hz), 7.03-7.35 (m, 2H), 7.66 (dd, 1H, $J_1$ = 8.0 Hz, $J_2$ = 1.6 Hz); $^{13}C$ NMR (100 MHz, $CDCl_3$) δ 25.44 ($CH_2$), 25.74 ($CH_2$), 26.19 ($CH_2$), 26.60 ($CH_2$), 27.05 ($CH_2$), 28.45 ($CH_2$), 28.86 ($CH_2$), 29.26 ($CH_2$), 29.31 ($CH_2$), 29.37 ($CH_2$), 39.32 ($CH_2$), 65.33 ($CH_2$), 66.55 ($CH_2$), 68.65 ($CH_2$), 75.56 (*C*H, observed in DEPT-90 NMR), 108.67 (=*C*H), 112.69 (=*C*H), 120.06 (=*C*H), 121.26 (*quat-C*), 122.68 (=*C*H), 125.01 (*quat-C*), 125.69 (=*C*H), 129.84 (=*C*H), 131.66 (=*C*H), 132.93 (=*C*H), 143.60 (*quat-C*), 157.88 (*quat-C*), 167.94 (*quat-C*), 174.40 (*quat-C*); HRMS (ESI) Calcd for $C_{29}H_{37}NO_5$ $[M+H]^+$ 480.2750; found, 480.2760.

*Crystal data for compound **12a**.* (CCDC 1005105) $C_{29}H_{37}NO_5$, $M$ = 479.60, 0.1 × 0.1 × 0.09 mm, Monoclinic, space group p121/c1 with $a$ = 8.8916(3) Å, $b$ = 34.6623(15) Å, $c$ =8.5392(3) Å, $\alpha$ = 90.00, $\beta$ = 96.831(2), $\gamma$ = 90.00, $V$ = 2613.13(17) $Å^3$, $T$ = 296.15 K, $R_1$ = 0.0848, w$R_2$ = 0.2800 on observed data, z = 4, $D_{calcd}$ = 1.219 mg $cm^{-3}$, *F(000)* = 1032, Absorption coefficient = 0.082 $mm^{-1}$, $\lambda$ = 0.71073 Å, 6948 reflections were collected on a smart apex CCD single crystal diffractometer 4125 observed reflections ($I \geq 2\sigma$ ($I$)). The largest difference peak and hole = 1.2580 and -0.5915 $eÅ^{-3}$, respectively. The structure was solved by direct methods and refined by full-matrix least squares on $F^2$ using SHELXL-97 software.

**Synthesis of macrocycle 12b.** Colorless solid (111 mg, 78%); mp 208-210 °C; IR (neat): $\nu_{max}$ 2924, 2853, 1714, 1695, 1608, 1598, 1486, 1466, 1365, 1215, 1190, 745 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) δ = 1.20-1.48 (m, 24H), 1.60-1.69 (m, 3H), 1.71-1.81 (m, 5H), 3.36-3.44 (m, 2H),

3.54-3.58 (m, 1H), 4.00 (t, 2H, $J$ = 6.0 Hz), 4.09-4.13 (m, 1H), 4.29 (td, 2H, $J_1$ = 6.8 Hz, $J_2$ = 1.2 Hz), 4.91 (s, 1H), 6.83 (d, 1H, $J$ = 8.0 Hz), 6.91-6.97 (m, 2H), 7.08 (t, 1H, $J$ = 7.6 Hz), 7.32 (t, 1H, $J$ = 8.0 Hz), 7.38-7.43 (m, 2H), 7.75 (dd, 1H, $J_1$ = 7.6 Hz, $J_2$ = 1.6 Hz); $^{13}$C NMR (100 MHz, $CDCl_3$) δ 25.85 (*C*H$_2$), 25.98 (*C*H$_2$), 26.38 (*C*H$_2$), 26.55 (*C*H$_2$), 27.01 (*C*H$_2$), 28.84 (*C*H$_2$), 29.22 (*C*H$_2$), 29.31 (*C*H$_2$), 29.37 (*C*H$_2$), 29.54 (*C*H$_2$), 29.60 (*C*H$_2$), 29.62 (*C*H$_2$), 29.83 (*C*H$_2$), 29.84 (*C*H$_2$), 29.88 (*C*H$_2$), 39.43 (*C*H$_2$), 65.16 (*C*H$_2$), 67.32 (*C*H$_2$), 68.77 (*C*H$_2$), 75.66 (*C*H, observed in DEPT-90 NMR), 108.83 (=*C*H), 112.83 (=*C*H), 119.97 (=*C*H), 121.11 (*quat-C*), 122.64 (=*C*H), 125.05 (*quat-C*), 125.55 (=*C*H), 129.81 (=*C*H), 131.64 (=*C*H), 133.02 (=*C*H), 143.76 (*quat-C*), 158.14 (*quat-C*), 167.77 (*quat-C*), 174.38 (*quat-C*); HRMS (ESI) Calcd for $C_{35}H_{49}NO_5$ $[M+H]^+$ 564.3689; found, 564.3681.

**Synthesis of macrocycle 12c.** Colorless solid (103 mg, 72%); mp 201-203 °C; IR (neat): $\nu_{max}$ 2922, 2856, 1714, 1665, 1565, 1456, 1336, 1263, 1081, 751 cm$^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$) δ = 1.29-1.20 (m, 11H), 1.32-1.39 (m, 7H), 1.55-1.70 (m, 10H), 3.28-3.36 (m, 2H), 3.38-3.42 (m, 1H), 3.92 (t, 2H, $J$ = 6 Hz), 4.04-4.11 (m, 1H), 4.18-4.22 (m, 2H), 4.88 (s, 1H), 6.76 (d, 1H, $J$ = 8.0 Hz), 6.83-6.89 (m, 2H), 7.01 (t, 1H, $J$ = 7.6 Hz), 7.25 (t, 1H, $J$ = 7.6 Hz), 7.31-7.35 (m, 2H), 7.67 (dd, 1H, $J_1$ = 7.6 Hz, $J_2$ = 2.0 Hz); $^{13}$C NMR (100 MHz, $CDCl_3$) δ 24.42 (*C*H$_2$), 25.24 (*C*H$_2$), 25.48 (*C*H$_2$), 26.10 (*C*H$_2$), 26.48 (*C*H$_2$), 26.78 (*C*H$_2$), 27.10 (*C*H$_2$), 27.68 (*C*H$_2$), 27.97 (*C*H$_2$), 28.25 (*C*H$_2$), 28.75 (*C*H$_2$), 29.36 (*C*H$_2$), 29.48 (*C*H$_2$), 29.78 (*C*H$_2$), 39.43 (*C*H$_2$), 65.15 (*C*H$_2$), 66.45 (*C*H$_2$), 68.66 (*C*H$_2$), 75.51 (*C*H, observed in DEPT-90 NMR), 108.62 (=*C*H), 112.49 (=*C*H), 120.16 (=*C*H), 121.46 (*quat-C*), 122.38 (=*C*H), 125.11 (*quat-C*), 125.73 (=*C*H), 129.80 (=*C*H), 131.46 (=*C*H), 132.18 (=*C*H), 143.30 (*quat-C*), 157.18 (*quat-C*), 167.14 (*quat-C*), 174.20 (*quat-C*); HRMS (ESI) Calcd for $C_{33}H_{45}NO_5$ $[M+H]^+$ 536.3376; found, 536.3384.

**Synthesis of macrocycle 12d.** Colorless solid (97 mg, 68%); mp 212-214 °C; IR (neat): $\nu_{max}$ 2956, 2845, 1709, 1682, 1612, 1592, 1483, 1478, 1334, 1210, 1171, 752 cm$^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$) δ = 1.23-1.41 (m, 20H), 1.48-1.61 (m, 4H), 1.67-1.78 (m, 4H), 3.56-3.68 (m, 2H), 3.72-3.81 (m, 1H), 3.92 (t, 2H, $J$ = 7.2 Hz), 4.02-4.13 (m, 1H), 4.20 (t, 2H, $J$ = 7.6 Hz), 4.87 (s, 1H), 6.76 (d, 1H, $J$ = 7.6 Hz), 6.82-6.91 (m, 2H), 7.10 (t, 1H, $J$ = 7.2 Hz), 7.31 (t, 1H, $J$ = 7.2 Hz), 7.36-7.42 (m, 2H), 7.61 (d, 1H, $J$ = 7.6 Hz); $^{13}$C NMR (100 MHz, $CDCl_3$) δ 25.63 (*C*H$_2$), 25.76 (*C*H$_2$), 26.18 (*C*H$_2$), 26.35 (*C*H$_2$), 26.89 (*C*H$_2$), 28.56 (*C*H$_2$), 28.92 (*C*H$_2$), 29.12 (*C*H$_2$), 29.23 (*C*H$_2$), 29.52 (*C*H$_2$), 29.68 (*C*H$_2$), 29.82 (*C*H$_2$), 29.88 (*C*H$_2$), 29.90 (*C*H$_2$), 38.29 (*C*H$_2$), 65.27 (*C*H$_2$), 66.78 (*C*H$_2$), 68.34 (*C*H$_2$), 75.54 (*C*H, observed in DEPT-90 NMR), 109.12 (=*C*H),

111.96 (=*C*H), 118.89 (=*C*H), 120.19 (*quat-C*), 121.34 (=*C*H), 124.12 (*quat-C*), 125.24 (=*C*H), 128.72 (=*C*H), 131.24 (=*C*H), 132.12 (=*C*H), 142.45 (*quat-C*), 156.67 (*quat-C*), 166.56 (*quat-C*), 175.25 (*quat-C*); HRMS (ESI) Calcd for $C_{33}H_{45}NO_5$ $[M+Na]^+$ 558.3195; found, 558.3190.

**General procedure for diazoamides 15**

To an oven-dried flask, a solution containing 3-diazooxindole **3** (200 mg, 1.25 mmol) and potassium carbonate (434 mg, 3.14 mmol) in dry DMF was taken under argon atmosphere. To this reaction mixture, a solution of appropriate bromoamine **14** (1.35 mmol) in dry DMF was slowly added over a period of 30 min and then a catalytic amount of tetrabutylammonium iodide. The progress of the reaction was monitored using TLC. The mixture was extracted with dichloromethane (3×25 mL) and the combined organic layers were washed with water (3×25 mL), brine (2×25 mL) and dried (anhydrous $Na_2SO_4$). The solvent was removed under reduced pressure and the resulting residue purified using column chromatography ($SiO_2$, hexane/ethyl acetate 85:15) to afford the respective diazoamides **15**.

**Synthesis of diazoamide 15a.** Red viscous liquid (473 mg, 78%); IR (neat): $\nu_{max}$ 3396, 2929, 2845, 2091, 1731, 1678, 1469, 1352, 1242, 729 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) δ = 1.24-1.28 (m, 7H), 1.32-1.39 (m, 2H), 1.58-1.65 (m, 3H), 1.67-1.74 (m, 2H), 3.73 (t, 2H, *J* = 7.6 Hz), 3.91 (t, 2H, *J* = 6.4 Hz), 4.26 (s, 2H), 6.60-6.65 (m, 3H), 6.79 (t, 2H, *J* = 7.8 Hz), 6.82-6.86 (m, 1H), 7.00 (td, 1H, $J_1$ = 7.8 Hz, $J_2$ = 0.8 Hz), 7.06-7.16 (m, 5H), 7.23 (dd, 1H, $J_1$ = 7.6 Hz, $J_2$ = 1.6 Hz); $^{13}C$ NMR (100 MHz, $CDCl_3$) δ 26.15 (*C*$H_2$), 26.85 (*C*$H_2$), 28.05 (*C*$H_2$), 29.21 (*C*$H_2$), 29.27 (*C*$H_2$), 29.40 (*C*$H_2$), 40.75 (*C*$H_2$), 44.06 (*C*$H_2$), 67.90 (*C*$H_2$), 108.90 (=*C*H), 111.09 (=*C*H), 113.63 (=*C*H), 116.88 (*quat-C*), 117.91 (=*C*H), 118.32 (=*C*H), 120.33 (=*C*H), 121.85 (=*C*H), 125.37 (=*C*H), 126.96 (*quat-C*), 128.36 (=*C*H), 129.07 (=*C*H), 129.16 (=*C*H), 133.93 (*quat-C*), 156.92 (*quat-C*), 166.73 (*quat-C*); HRMS (ESI) Calcd for $C_{30}H_{34}N_4O_2$ $[M+Na]^+$ 505.2579; found, 505.2586.

**Synthesis of diazoamide 15b.** Red viscous liquid (468 mg, 75%); IR (neat): $\nu_{max}$ 3393, 2926, 2854, 2094, 1720, 1603, 1461, 1358, 1240, 750 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) δ = 1.18-1.36 (m, 12H), 1.58-1.71 (m, 4H), 3.74 (t, 2H, *J* = 7.6 Hz), 3.85 (t, 2H, *J* = 6.8 Hz), 4.22 (s, 2H), 6.61 (d, 2H, *J* = 8.0 Hz), 6.66-6.73 (m, 2H), 6.86 (d, 3H, *J* = 7.6 Hz), 7.00 (t, 1H, *J* = 7.6 Hz), 7.08-7.18 (m, 5H); $^{13}C$ NMR (100 MHz, $CDCl_3$) δ 26.30 (*C*$H_2$), 26.75 (*C*$H_2$), 28.15 (*C*$H_2$), 28.33 (*C*$H_2$), 29.14 (*C*$H_2$), 29.64 (*C*$H_2$), 29.89 (*C*$H_2$), 40.24 (*C*$H_2$), 44.16 (*C*$H_2$), 66.98 (*C*$H_2$), 108.96 (=*C*H), 111.43 (=*C*H), 113.80 (=*C*H), 116.15 (*quat-C*), 117.89 (=*C*H), 118.10 (=*C*H), 120.67

(=*C*H), 121.15 (=*C*H), 125.77 (=*C*H), 126.46 (*quat-C*), 128.16 (=*C*H), 128.87 (=*C*H), 129.26 (=*C*H), 133.43 (*quat-C*), 156.12 (*quat-C*), 166.43 (*quat-C*); Anal. Calcd for $C_{31}H_{36}N_4O_2$ (496.64): C, 74.97; H, 7.31; N, 11.28. Found: C, 74.86; H, 7.29; N, 11.23.

**Synthesis of diazoamide 15c.** Red viscous liquid (455 mg, 73%); IR (neat): $\nu_{max}$ 3392, 2927, 2855, 2093, 1722, 1681, 1461, 1356, 1238, 726 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) δ = 1.21-1.27 (m, 10H), 1.34-1.37 (m, 2H), 1.58-1.63 (m, 2H), 1.68-1.73 (m, 2H), 3.73 (t, 2H, *J* = 7.2 Hz), 3.91 (t, 2H, *J* = 6.4 Hz), 4.27 (s, 2H), 6.63-6.67 (m, 3H), 6.79 (t, 2H, *J* = 8.0 Hz), 6.83-6.87 (m, 1H), 6.98-7.02 (m, 1H), 7.07-7.16 (m, 5H), 7.24 (d, 1H, *J* = 7.2 Hz); $^{13}C$ NMR (100 MHz, $CDCl_3$) δ 26.34 (*C*$H_2$), 26.85 (*C*$H_2$), 28.10 (*C*$H_2$), 28.12 (*C*$H_2$), 28.67 (*C*$H_2$), 29.12 (*C*$H_2$), 29.96 (*C*$H_2$), 40.14 (*C*$H_2$), 44.56 (*C*$H_2$), 66.78 (*C*$H_2$), 108.66 (=*C*H), 111.23 (=*C*H), 113.64 (=*C*H), 116.80 (*quat-C*), 117.45 (=*C*H), 118.73 (=*C*H), 120.43 (=*C*H), 124.76 (=*C*H), 126.26 (*quat-C*), 128.86 (=*C*H), 129.17 (=*C*H), 129.56 (=*C*H), 133.23 (*quat-C*), 156.42 (*quat-C*), 166.73 (*quat-C*); Anal. Calcd for $C_{31}H_{36}N_4O_2$ (496.64): C, 74.97; H, 7.31; N, 11.28. Found: C, 75.10; H, 7.35; N, 11.32.

**General procedure for macrocycles 16.** A solution of diazoamide **15** (150 mg, 1.0 mmol) and rhodium(II) acetate dimer (1.0 mol%) in dichloromethane (15 mL) was stirred at room temperature for 15-20 min. The progress of the reaction was monitored using TLC. After completing of the reaction, reaction mixture was concentrated under reduced pressure and purified using column chromatography ($SiO_2$, hexane/ethyl acetate 75:25) to afford the respective macrocycle **16**.

**Synthesis of macrocycle 16a.** Colorless solid (96 mg, 68%); mp 215-217 °C; IR (neat): $\nu_{max}$ 2923, 2851, 1715, 1598, 1504, 1487, 1463, 1346, 1227, 1152, 751 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) δ = 1.18-1.35 (m, 10H), 1.59-1.71 (m, 4H), 3.38 (d, 1H, *J* = 13.6 Hz), 3.65 (d, 1H, *J* = 16.8 Hz), 3.77-3.83 (m, 1H), 3.97-4.07 (m, 2H), 4.67 (d, 1H, $J_1$ = 17.2 Hz), 5.53 (s, 1H), 6.66-6.71 (m, 2H), 6.74-6.78 (m, 2H), 6.84 (d, 2H, *J* = 8.4 Hz), 6.91 (t, 1H, *J* = 7.6 Hz), 7.03-7.12 (m, 3H), 7.18 (t, 1H, *J* = 8.4 Hz), 7.36 (d, 2H, *J* = 7.2 Hz); $^{13}C$ NMR (100 MHz, $CDCl_3$) δ 24.79 (*C*$H_2$), 26.545 (*C*$H_2$), 26.548 (*C*$H_2$), 26.99 (*C*$H_2$), 27.52 (*C*$H_2$), 27.88 (*C*$H_2$), 27.95 (*C*$H_2$), 38.66 (*C*$H_2$), 45.50 (*C*$H_2$), 62.05 (*C*H, observed in DEPT-90 NMR), 67.23 ($CH_2$), 107.80 (=*C*H), 109.14 (=*C*H), 114.25 (=*C*H), 117.52 (=*C*H), 119.02 (=*C*H), 121.49 (=*C*H), 124.12 (*quat-C*), 125.05 (=*C*H), 125.34 (=*C*H), 126.40 (=*C*H), 126.86 (*quat-C*), 127.99 (=*C*H), 128.12 (=*C*H),

142.31 (*quat-C*), 147.94 (*quat-C*), 154.87 (*quat-C*), 173.38 (*quat-C*); HRMS (ESI) Calcd for $C_{30}H_{34}N_2O_2$ $[M+H]^+$ 455.2699; found, 455.2707.

**Synthesis of macrocycle 16b.** Colorless solid (102 mg, 72%); mp 216-218 °C; IR (neat): $\nu_{max}$ 2923, 2854, 1714, 1609, 1597, 1503, 1487, 1465, 1277, 1222, 1047, 742 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) δ = 1.28-1.41 (m, 12H), 1.69-1.74 (m, 4H), 3.41-3.47 (m, 1H), 3.85 (d, 1H, *J* = 17.6 Hz, C*H*$_2$), 3.90-4.01 (m, 2H), 4.09-4.16 (m, 1H), 4.60 (d, 1H, *J* = 17.6 Hz), 5.67 (s, 1H), 6.78-6.81 (m, 2H), 6.87-6.94 (m, 4H), 6.98 (t, 1H, *J* = 7.6 Hz), 7.14-7.22 (m, 3H), 7.29 (t, 1H, *J* = 8.4 Hz), 7.40 (d, 1H, *J* = 7.2 Hz), 7.50 (d, 1H, *J* = 7.6 Hz); $^{13}C$ NMR (100 MHz, $CDCl_3$) δ 24.73 (*C*H$_2$), 26.02 (*C*H$_2$), 26.14 (*C*H$_2$), 26.43 (*C*H$_2$), 26.64 (*C*H$_2$), 26.93 (*C*H$_2$), 27.11 (*C*H$_2$), 28.55 (*C*H$_2$), 39.80 (*C*H$_2$), 46.60 (*C*H$_2$), 62.44 (*C*H, observed in DEPT-90 NMR), 67.39 (*C*H$_2$), 108.77 (=*C*H), 110.29 (=*C*H), 115.24 (=*C*H), 118.50 (=*C*H), 120.12 (=*C*H), 122.51 (=*C*H), 125.11 (=*C*H), 125.88 (*quat-C*), 126.32 (*quat-C*), 127.42 (=*C*H), 128.08 (=*C*H), 129.01 (=*C*H), 129.18 (=*C*H), 143.59 (*quat-C*), 148.75 (*quat-C*), 155.98 (*quat-C*), 174.67 (*quat-C*); HRMS (ESI) Calcd for $C_{31}H_{36}N_2O_2$ $[M+H]^+$ 469.2855; found, 469.2858.

**Synthesis of macrocycle 16c.** Colorless solid (90 mg, 64%); mp 203-205 °C; IR (neat): $\nu_{max}$ 2928, 2853, 1720, 1608, 1503, 1462, 1344, 1230, 746 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) δ = 1.62-1.69 (m, 8H), 1.73-1.81 (m, 4H), 1.99-2.05 (m, 4H), 3.76 (d, 1H, *J* = 17.6 Hz), 3.82-3.89 (m, 2H), 4.12-4.23 (m, 2H), 4.42 (d, 1H, *J* = 17.6 Hz), 5.58 (s, 1H), 6.67-6.78 (m, 2H), 6.81-6.89 (m, 4H), 6.92 (d, 1H, *J* = 7.2 Hz), 7.02-7.12 (m, 2H), 7.31 (t, 2H, *J* = 7.6 Hz), 7.36 (t, 1H, *J* = 7.6 Hz), 7.42 (d, 1H, *J* = 7.2 Hz); $^{13}C$ NMR (100 MHz, $CDCl_3$) δ 25.92 (*C*H$_2$), 26.08 (*C*H$_2$), 26.12 (*C*H$_2$), 26.36 (*C*H$_2$), 26.78 (*C*H$_2$), 26.90 (*C*H$_2$), 27.16 (*C*H$_2$), 28.89 (*C*H$_2$), 39.92 (*C*H$_2$), 40.61 (*C*H$_2$), 62.86 (CH, observed in DEPT-90 NMR), 67.12 (*C*H$_2$), 109.34 (=*C*H), 110.12 (=*C*H), 113.65 (=*C*H), 116.75 (=*C*H), 121.46 (=*C*H), 124.64 (=*C*H), 125.17 (*quat-C*), 126.31 (*quat-C*), 127.40 (=*C*H), 128.02 (=*C*H), 129.10 (=*C*H), 129.28 (=*C*H), 144.67 (*quat-C*), 149.64 (*quat-C*), 156.12 (*quat-C*), 176.23 (*quat-C*); HRMS (ESI) Calcd for $C_{31}H_{36}N_2O_2$ $[M+Na]^+$ 491.2674; found, 491.2668.

**General procedure for diazoamides 18**

To an oven-dried flask, a solution containing 3-diazooxindole **3** (200 mg, 1.25 mmol) and potassium carbonate (434 mg, 3.14 mmol) in dry DMF was taken under argon atmosphere. To this reaction mixture, a solution of appropriate bromoalcohol **17** (1.35 mmol) in dry DMF was slowly added over a period of 30 min and then a catalytic amount of tetrabutylammonium iodide.

The progress of the reaction was monitored using TLC. The mixture was extracted with dichloromethane (3×25 mL) and the combined organic layers were washed with water (3×25 mL), brine (2×25 mL) and dried (anhydrous $Na_2SO_4$). The solvent was removed under reduced pressure and the resulting residue purified using column chromatography ($SiO_2$, hexane/ethyl acetate 85:15) to afford diazoamides **18**.

**Synthesis of diazoamide 18a.** Red viscous liquid (205 mg, 75%); IR (neat): $\nu_{max}$ 3420, 2921, 2851, 2093, 1653, 1612, 1454, 1390, 1165, 1070, 738 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) δ = 1.86-1.92 (m, 2H), 3.33 (s, 1H), 3.58 (s, 2H), 4.01 (t, 2H, *J* = 6.4 Hz), 6.99 (d, 1H, *J* = 8 Hz), 7.11 (td, 1H, $J_1$ = 7.6 Hz, $J_2$ = 0.8 Hz), 7.19-7.24 (m, 2H); $^{13}C$ NMR (100 MHz, $CDCl_3$) δ 30.36 (*C*$H_2$), 36.82 (*C*$H_2$), 58.29 (*C*$H_2$), 108.95 (=*C*H), 116.94 (*quat-C*), 118.44 (=*C*H), 122.35 (=*C*H), 125.63 (=*C*H), 133.40 (*quat-C*), 167.84 (*quat-C*); Anal. Calcd for $C_{11}H_{11}N_3O_2$ (217.22): C, 60.82; H, 5.10; N, 19.34. Found: C, 60.98; H, 5.15; N, 19.39.

**Synthesis of diazoamide 18b.** Red viscous liquid (212 mg, 73%); IR (neat): $\nu_{max}$ 3425, 2929, 2858, 2091, 1659, 1610, 1462, 1395, 1187, 1089, 745 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) δ = 1.76-1.84 (m, 2H), 1.88-1.95 (m, 2H), 3.65 (s, 1H), 3.72 (s, 2H), 3.98 (t, 2H, *J* = 7.2 Hz), 6.78 (d, 1H, *J* = 7.6 Hz), 7.17 (td, 1H, $J_1$ = 7.2 Hz, $J_2$ = 1.2 Hz), 7.23-7.28 (m, 2H); $^{13}C$ NMR (100 MHz, $CDCl_3$) δ 27.46 (*C*$H_2$), 30.28 (*C*$H_2$), 36.43 (*C*$H_2$), 58.02 (*C*$H_2$), 108.19 (=*C*H), 116.46 (*quat-C*), 118.38 (=*C*H), 122.24 (=*C*H), 125.81 (=*C*H), 133.29 (*quat-C*), 167.89 (*quat-C*); Anal. Calcd for $C_{12}H_{13}N_3O_2$ (231.25): C, 62.33; H, 5.67; N, 18.17. Found: C, 62.39; H, 5.64; N, 18.20.

**Synthesis of diazoamide 18c.** Red viscous liquid (189 mg, 65%); IR (neat): $\nu_{max}$ 3422, 2924, 2857, 2094, 1665, 1608, 1464, 1398, 1184, 1040, 747 $cm^{-1}$; $[\alpha]^{26}_D$ = -12.20 (*c* 0.1, MeOH); $^1H$ NMR (400 MHz, $CDCl_3$) δ = 1.04 (d, 3H, *J* = 7.2 Hz), 1.23-1.33 (m, 1H), 2.06 (br, s, 1H), 3.38 (dd, 1H, $J_1$ = 11.6 Hz, $J_2$ = 5.2 Hz), 3.51 (dd, 1H, $J_1$ = 11.6 Hz, $J_2$ = 5.2 Hz), 3.73 (dd, 1H, $J_1$ = 14.4 Hz, $J_2$ = 5.2 Hz), 3.93 (dd, 1H, $J_1$ = 14.4 Hz, $J_2$ = 8.4 Hz), 7.00 (d, 1H, *J* = 7.6 Hz), 7.11 (t, 1H, *J* = 7.6 Hz), 7.19-7.26 (m, 2H); $^{13}C$ NMR (100 MHz, $CDCl_3$) δ 14.98 (*C*$H_3$), 35.08 (*C*H), 42.83 (*C*$H_2$), 63.62 (*C*$H_2$), 109.31 (=*C*H), 116.85 (*quat-C*), 118.35 (=*C*H), 122.36 (=*C*H), 125.60 (=*C*H), 134.00 (*quat-C*), 168.11 (*quat-C*); Anal. Calcd for $C_{12}H_{13}N_3O_2$ (231.25): C, 62.33; H, 5.67; N, 18.17. Found: C, 62.25; H, 5.72; N, 18.11.

**Synthesis of diazoamide 18d.** Red viscous liquid (201 mg, 68%); IR (neat): $\nu_{max}$ 3424, 2943, 2845, 2098, 1650, 1613, 1459, 1389, 1174, 1075, 731 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) δ = 1.74-1.87 (m, 2H), 3.67 (br, s, 1H), 3.89 (s, 2H), 4.13 (t, 2H, *J* = 7.0 Hz), 6.78 (d, 1H, *J* = 8 Hz),

7.11-7.18 (m, 1H), 7.24-7.29 (m, 1H); $^{13}$C NMR (100 MHz, $CDCl_3$) δ 28.96 (*C*$H_2$), 37.82 (*C*$H_2$), 56.29 (*C*$H_2$), 107.45 (=*C*H), 117.78 (*quat-C*), 118.89 (*quat-C*), 121.45 (=*C*H), 126.78 (=*C*H), 134.78 (*quat-C*), 168.90 (*quat-C*); Anal. Calcd for $C_{11}H_{10}ClN_3O_2$ (251.67): C, 52.50; H, 4.01; N, 16.70. Found: C, 52.67; H, 4.07; N, 16.64.

**Synthesis of diazoamide 18e.** Red viscous liquid (180 mg, 60%); IR (neat): $\nu_{max}$ 3424, 2920, 2850, 2089, 1661, 1603, 1465, 1389, 1134, 1024, 735 cm$^{-1}$; $[\alpha]^{26}_D$ = -16.34 (*c* 0.1, MeOH); $^1$H NMR (400 MHz, $CDCl_3$) δ = 1.15 (d, 3H, *J* = 7.6 Hz), 1.27-1.35 (m, 1H), 2.12 (br, s, 1H), 3.48 (dd, 1H, $J_1$ = 11.6 Hz, $J_2$ = 5.2 Hz), 3.57 (dd, 1H, $J_1$ = 11.6 Hz, $J_2$ = 5.2 Hz), 3.86 (dd, 1H, $J_1$ = 14.6 Hz, $J_2$ = 5.2 Hz), 3.98 (dd, 1H, $J_1$ = 14.6 Hz, $J_2$ = 8.4 Hz), 7.14 (d, 1H, *J* = 8.0 Hz), 7.31-7.37 (m, 2H); $^{13}$C NMR (100 MHz, $CDCl_3$) δ 14.97 (*C*$H_3$), 35.34 (*C*H), 42.67 (*C*$H_2$), 63.67 (*C*$H_2$), 108.23 (=*C*H), 117.89 (*quat-C*), 117.34 (=*C*H), 124.67 (=*C*H), 126.30 (=*C*H), 133.23 (*quat-C*), 169.23 (*quat-C*); Anal. Calcd for $C_{12}H_{12}ClN_3O_2$ (265.70): C, 54.25; H, 4.55; N, 15.82. Found: C, 54.31; H, 4.52; N, 15.79.

**Synthesis of diazoamide 18f.** Red viscous liquid (199 mg, 78%); IR (neat): $\nu_{max}$ 3421, 2924, 2854, 2090, 1657, 1608, 1466, 1398, 1177, 1078, 733 cm$^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$) δ = 2.84 (s, 1H), 3.91 (t, 2H, *J* = 5.2 Hz), 3.98 (t, 2H, *J* = 5.2 Hz), 7.03 (d, 1H, *J* = 7.6 Hz), 7.09 (t, 1H, *J* = 7.2 Hz), 7.17-7.21 (m, 2H); $^{13}$C NMR (100 MHz, $CDCl_3$) δ 43.80 (*C*$H_2$), 60.99 (*C*$H_2$), 109.20 (=*C*H), 116.78 (*quat-C*), 118.31 (=*C*H), 122.27 (=*C*H), 125.56 (=*C*H), 133.98 (*quat-C*), 167.77 (*quat-C*); Anal. Calcd for $C_{10}H_9N_3O_2$ (203.20): C, 59.11; H, 4.46; N, 20.68. Found: C, 59.27; H, 4.52; N, 20.73.

**Synthesis of diazoamide 18g.** Red viscous liquid (265 mg, 70%); IR (neat): $\nu_{max}$ 3456, 2989, 2856, 2095, 1634, 1615, 1423, 1390, 1134, 1078, 740 cm$^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$) δ = 1.62-1.87 (m, 2H), 1.89-1.97 (m, 4H), 3.65-3.75 (m, 2H), 3.79 (br, s, 2H), 3.96 (t, 2H, *J* = 7.2 Hz), 6.74 (d, 1H, *J* = 7.6 Hz), 7.45 (td, 1H, $J_1$ = 7.2 Hz, $J_2$ = 1.2 Hz), 7.55-7.67 (m, 2H); $^{13}$C NMR (100 MHz, $CDCl_3$) δ 26.46 (*C*$H_2$), 26.67 (*C*$H_2$), 30.20 (*C*$H_2$), 36.34 (*C*$H_2$), 38.78 (*C*$H_2$), 58.78 (*C*$H_2$), 108.34 (=*C*H), 116.67 (*quat-C*), 117.45 (=*C*H), 121.67 (=*C*H), 124.23 (=*C*H), 132.45 (*quat-C*), 168.81 (*quat-C*); Anal. Calcd for $C_{14}H_{17}N_3O_2$ (259.30): C, 64.85; H, 6.61; N, 16.20. Found: C, 64.71; H, 6.54; N, 16.13.

**General procedure for macrocycles 19.** A solution of diazoamide **18** (100 mg, 1.0 mmol) and rhodium(II) acetate dimer (1.0 mol%) in dichloromethane (15 mL) was stirred at room temperature for 15-20 min. The progress of the reaction was monitored using TLC. After

completion of the reaction, reaction mixture was concentrated under reduced pressure and purified using column chromatography ($SiO_2$, hexane/ethyl acetate 75:25) to afford the macrocycles **19**.

**Synthesis of macrocycle 19a.** Colorless solid (45 mg, 52%); mp 211-213 °C; IR (neat): $\nu_{max}$ 2932, 2856, 1721, 1609, 1513, 1478, 1340, 1234, 754 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) δ = 1.98-2.02 (m, 1H), 2.11-2.20 (m, 1H), 2.69-2.75 (m, 1H), 3.36 (dt, 1H, $J_1$ = 14.8 Hz, $J_2$ = 3.2 Hz), 3.46-3.50 (m, 1H), 3.93-4.01 (m, 1H), 4.93 (s, 1H), 6.84 (d, 1H, $J$ = 8 Hz), 7.12 (td, 1H, $J_1$ = 7.6 Hz, $J_2$ = 0.4 Hz), 7.36 (t, 1H, $J$ = 7.6 Hz), 7.40 (d, 1H, $J$ = 7.2 Hz); $^{13}C$ NMR (100 MHz, $CDCl_3$) δ 27.75 (*C*$H_2$), 35.76 (*C*$H_2$), 64.46 (*C*$H_2$), 76.08 (*C*H), 109.07 (=*C*H), 123.29 (=*C*H), 123.90 (*quat-C*), 125.83 (=*C*H), 130.45 (=*C*H), 142.80 (*quat-C*), 174.49 (*quat-C*); HRMS (ESI) Calcd for $C_{22}H_{22}N_2O_4$ $[M+H]^+$ 379.1658; found, 379.1664.

*Crystal data for compound **19a**.* (CCDC 1005106) $C_{22}H_{22}N_2O_4$, $M$ = 378.42, 0.09 × 0.08 × 0.04 mm, Triclinic, space group p-1 with $a$ = 7.9479(2) Å, $b$ = 9.0065(2) Å, $c$ = 14.4450(3) Å, $\alpha$ = 75.800(10), $\beta$ = 77.803(10), $\gamma$ = 72.644(10), $V$ = 946.06(4) $Å^3$, $T$ = 296(2) K, $R_1$ = 0.0528, w$R_2$ = 0.1785 on observed data, z = 2, $D_{calcd}$ = 1.328 mg $cm^{-3}$, *F(000)* = 400, Absorption coefficient =0.092 $mm^{-1}$, $\lambda$ = 0.71073 Å, 5847 reflections were collected on a smart apex CCD single crystal diffractometer 3812 observed reflections ($I \geq 2\sigma(I)$). The largest difference peak and hole = 0.258 and -0.214 e$Å^{-3}$, respectively. The structure was solved by direct methods and refined by full-matrix least squares on $F^2$ using SHELXL-97 software.

**Synthesis of macrocycle 19b.** Colorless solid (44 mg, 50%); mp 198-200 °C; IR (neat): $\nu_{max}$ 2929, 2852, 1725, 1613, 1510, 1468, 1331, 1230, 764 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) δ = 1.67-1.77 (m, 1H), 1.79-1.85 (m, 1H), 1.89-2.07 (m, 1H), 2.19-2.32 (m, 1H), 2.81-2.92 (m, 1H), 3.42-3.49 (m 1H), 3.68-3.75 (m, 1H), 3.98-4.12 (m, 1H), 5.03 (s, 1H), 6.78 (d, 1H, $J$ = 7.2 Hz), 7.35 (t, 1H, $J$ = 7.2 Hz), 7.42 (t, 1H, $J$ = 8.0 Hz), 7.47 (d, 1H, $J$ = 7.6 Hz); $^{13}C$ NMR (100 MHz, $CDCl_3$) δ 27.25 (*C*$H_2$), 27.86 (*C*$H_2$), 35.24 (*C*$H_2$), 64.37 (*C*$H_2$), 76.12 (*C*H), 109.23 (=*C*H), 123.32 (=*C*H), 123.98 (*quat-C*), 125.87 (=*C*H), 130.41 (=*C*H), 142.86 (*quat-C*), 174.67 (*quat-C*); HRMS (ESI) Calcd for $C_{24}H_{26}N_2O_4$ $[M+H]^+$ 407.1971; found, 407.1967.

**Synthesis of macrocycle 19c.** Colorless solid (39 mg, 45%); mp 210-212 °C; IR (neat): $\nu_{max}$ 2921, 2847, 1729, 1617, 1515, 1460, 1325, 1256, 753 $cm^{-1}$; $[\alpha]^{31}_D$ = 46.36 (*c* 0.05, MeOH); $^1H$ NMR (400 MHz, $CDCl_3$) δ = 1.07 (d, 3H, $J$ = 6.8 Hz), 2.22-2.31 (m, 1H), 3.10 (dd, 1H, $J_1$ = 14.4 Hz, $J_2$ = 4.0 Hz), 3.43-3.47 (m, 1H), 3.84-3.98 (m, 2H), 4.53 (s, 1H), 6.44 (d, 1H, $J$ = 7.6 Hz),

6.80 (t, 1H, $J$ = 7.2 Hz), 6.91 (d, 1H, $J$ = 7.2 Hz), 7.07 (t, 1H, $J$ = 8 Hz); $^{13}$C NMR (100 MHz, $CDCl_3$) δ 15.24 (*C*H$_3$), 31.73 (*C*H), 43.65 (*C*H$_2$), 73.33 (*C*H$_2$), 75.95 (*C*H), 108.62 (=*C*H), 121.94 (=*C*H), 124.85 (=*C*H), 125.29 (*quat-C*), 129.25 (=*C*H), 143.40 (*quat-C*), 174.43 (*quat-C*); HRMS (ESI) Calcd for $C_{24}H_{26}N_2O_4$ $[M+H]^+$ 407.1971; found, 407.1976.

**Synthesis of macrocycle 19d.** Colorless solid (39 mg, 44%); mp 211-213 °C; IR (neat): $\nu_{max}$ 2932, 2856, 1721, 1609, 1513, 1478, 1340, 1234, 754 cm$^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$) δ = 1.86-1.91 (m, 1H), 2.17-2.23 (m, 1H), 3.27-3.32 (m, 1H), 3.65-3.69 (m, 1H), 4.24-4.35 (m, 2H), 4.37 (s, 1H), 6.55 (d, 1H, $J$ = 8.4 Hz), 6.82 (d, 1H, $J$ = 1.2 Hz), 7.17 (dd, 1H, $J_1$ = 8.0 Hz, $J_2$ = 2.0 Hz); $^{13}$C NMR (100 MHz, $CDCl_3$) δ 26.89 (*C*H$_2$), 37.65 (*C*H$_2$), 68.55 (*C*H$_2$), 75.43 (*C*H), 109.73 (=*C*H), 125.19 (=*C*H), 126.87 (*quat-C*), 127.44 (*quat-C*), 128.97 (=*C*H), 142.09 (*quat-C*), 174.78 (C=O); HRMS (ESI) Calcd for $C_{22}H_{20}Cl_2N_2O_4$ $[M+H]^+$ 447.0878; found, 447.0890.

**Synthesis of macrocycle 19e.** Colorless solid (36 mg, 40%); mp 220-222 °C; IR (neat): $\nu_{max}$ 2931, 2887, 1745, 1667, 1556, 1423, 1390, 1222, 750 cm$^{-1}$; $[\alpha]^{31}_D$ = 42.56 (*c* 0.05, MeOH); $^1$H NMR (400 MHz, $CDCl_3$) δ = 1.06 (d, 3H, $J$ = 6.8 Hz), 2.29-2.37 (m, 1H), 3.17 (dd, 1H, $J_1$ = 14.4 Hz, $J_2$ = 4.0 Hz), 3.42-3.46 (m, 1H), 3.98-4.04 (m, 2H), 4.41 (s, 1H), 6.51 (d, 1H, $J$ = 8.4 Hz), 6.81 (s, 1H), 7.17 (d, 1H, $J$ = 2.0 Hz); $^{13}$C NMR (100 MHz, $CDCl_3$) δ 15.46 (*C*H$_3$), 32.98 (*C*H), 44.23 (*C*H$_2$), 72.67 (*C*H$_2$), 75.34 (*C*H), 107.34 (=*C*H), 122.45 (*quat-C*), 123.35 (=*C*H), 126.09 (*quat-C*), 130.85 (=*C*H), 142.67 (*quat-C*), 173.83 (*quat-C*); HRMS (ESI) Calcd for $C_{24}H_{24}Cl_2N_2O_4$ $[M+H]^+$ 475.1191; found, 475.1176.

**Synthesis of macrocycle 20g:** Colorless liquid (3.5 mg, 4%); IR (neat): $\nu_{max}$ 2931, 2799, 1721, 1512, 1480, 1310, 1223, 709 cm$^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$) δ = 1.41-1.73 (m, 6H), 3.28-3.38 (m, 4H), 3.40-3.53 (m, 2H), 4.92 (s, 1H), 6.83 (d, 1H, $J$ = 7.6 Hz), 7.08 (t, 1H, $J$ = 7.6 Hz), 7.06-7.34 (m, 1H), 7.40 (d, 1H, $J$ = 7.2 Hz); $^{13}$C NMR (100 MHz, $CDCl_3$) δ 26.12 (*C*H$_2$), 27.43 (*C*H$_2$), 28.16 (*C*H$_2$), 28.78 (*C*H$_2$), 33.61 (*C*H$_2$), 64.12 (*C*H$_2$), 76.12 (*C*H), 105.12 (=*C*H), 122.13 (=*C*H), 124.56 (*quat-C*), 126.07 (=*C*H), 132.34 (=*C*H), 142.23 (*quat-C*), 172.98 (*quat-C*); HRMS (ESI) Calcd for $C_{14}H_{17}NO_2$ $[M+H]^+$ 232.1338; found, 232.1329.

**Synthesis of macrocycle 21a.** Colorless solid (17 mg, 20%); mp 230-232 °C; IR (neat): $\nu_{max}$ 2944, 2860, 1726, 1619, 1545, 1487, 1311, 1230, 748 cm$^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$) δ = 1.54-1.65 (m, 8H), 3.29-3.43 (m, 3H), 3.99-4.06 (m, 1H), 4.88 (s, 1H), 6.81 (d, 1H, $J$ = 7.8 Hz), 7.07 (t, 1H, $J$ = 7.4 Hz), 7.29-7.35 (m, 2H); $^{13}$C NMR (100 MHz, $CDCl_3$) δ 26.89 (*C*H$_2$), 27.34 (*C*H$_2$), 28.06 (*C*H$_2$), 29.86 (*C*H$_2$), 35.67 (*C*H$_2$), 63.75 (*C*H$_2$), 77.43 (*C*H), 108.67 (=*C*H), 123.78

(=*C*H), 123.81 (*quat-C*), 126.47 (=*C*H), 133.11 (=*C*H), 143.56 (*quat-C*), 173.67 (*quat-C*); HRMS (ESI) Calcd for $C_{28}H_{34}N_2O_4$ $[M+H]^+$ 463.2597; found, 463.2578.

**Synthesis of macrocycle 21b:** Colorless liquid (10 mg, 11%); IR (neat): $\nu_{max}$ 2932, 2862, 1725, 1610, 1543, 1486, 1343, 1256, 740 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) δ = 1.31-1.38 (m, 2H), 1.52-1.67 (m, 6H), 3.32-3.41 (m, 3H), 4.01-4.08 (m, 1H), 4.89 (s, 1H), 6.74 (d, 1H, *J* = 7.8 Hz), 6.98 (t, 1H, *J* = 7.4 Hz), 7.21 (t, 1H, *J* = 7.6 Hz), 7.31 (d, 1H, *J* = 7.2 Hz); $^{13}C$ NMR (100 MHz, $CDCl_3$) δ 26.87 ($CH_2$), 27.36 ($CH_2$), 28.11 ($CH_2$), 29.98 ($CH_2$), 35.69 ($CH_2$), 63.78 ($CH_2$), 77.46 (*C*H), 108.70 (=*C*H), 123.82 (=*C*H), 123.86 (*quat-C*), 126.51 (=*C*H), 133.13 (=*C*H), 143.57 (*quat-C*), 173.75 (*quat-C*); HRMS (ESI) Calcd for $C_{28}H_{34}N_2O_4$ $[M+H]^+$ 463.2597; found, 463.2586.

**Supporting Information** (see footnote on the first page of this article): Copies of $^1H$ NMR and $^{13}C$ NMR spectra of all the isolated new compounds. X-ray crystal (CCDC 1005105-1005106) packing of **12a** and **19a**. This material is available free of charge *via* the Internet at http://pubs.acs.org.

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16 See supporting information for more details

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19 The minimization energy was found to be 7.17 kcal/mole more for **19f** when compared to **19a** based on MM2 calculations.